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TROPICAL DISEASES BULLETIN

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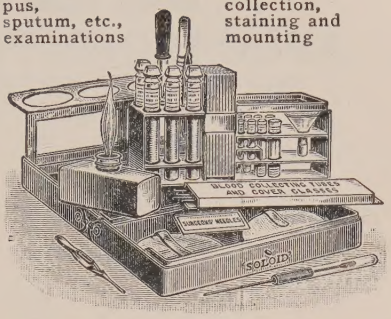

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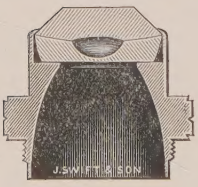

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TROPICAL DISEASES BULLETIN.

Vol. 2.] 1913. [No. 7.

MALARIA.

HODGSON (E. C.). **Report on the Work of the Central Malaria Bureau, 1911-12.**—*Proceedings of the Third Meeting of the General Malaria Committee held at Madras,* Nov. 18, 19, 20, 1912. pp. 51-52. (1913. Simla: Govt. Central Branch Press.)

The work of the Bureau has resulted in securing a complete set of all known Indian Anopheles and has aimed at getting together as many duplicate sets as possible for teaching purposes. Larvae-eating fish have been secured and identified and new specimens have been added to the collection at the Bureau. A list of these is given. In addition specimens of duckweed of four species have been collected. These by growing in a thick layer on the surface of pools are said to hinder the growth of larvae. [In Algeria experiments in this direction with *Azolla* (Salviniaceae) did not succeed.]

Andrew Balfour.

BENTLEY (C. A.). i. **A New Conception regarding Malaria.** ii. **Some Problems presented by Malaria in Bengal.**—*Ibid.* pp. 61-70 and 71-84.

i. An epidemiological paper which advances a plea for a broader outlook, not only in the case of malaria but in all parasitic diseases. The author insists on the recognition of the difference between malarial infection and malarial disease. The former, *i.e.*, mere infestation by malarial parasites, is, he says, often as natural amongst primitive races as flea infestation is to a dog. He holds the theory that the occurrence of *epidemic* disease is always the result of a serious change in environment converting favourable into unfavourable conditions. Such changes may be due to the introduction of an unfamiliar parasite, the influence of unusual seasons, or the result of the great disturbances produced among primitive parasite-harbouring races by advancing civilisation. In this connection he cites the history of England and of Holland, both as regards malaria and other diseases. So far as malaria is concerned the paramount influence

(31591—2.) Wt. P 1376—9. 1800. 9/13. D & S.

in these countries was the improvement in agriculture, and this is what is chiefly required for dealing with rural malaria in India.

To this end the cultivating classes of the population should be educated, their standard of comfort improved and attempts should be made to induce capitalists to undertake agricultural operations on a large scale. The author thinks the function of the State lies mainly in providing for the education of the population, as though it may initiate reforms, the people must carry these into active practice and without their intelligent co-operation no scheme of improved sanitation can be made effective.

He believes that eventually civilisation and its attendant blessings will banish malaria from India as certainly as it freed England from this scourge of former days.

ii. There are areas in Bengal which have been largely depopulated and where malaria is common and severe. Bentley finds that the prevalence of fever is not due, as has been thought, to water-logging of the soil but is the result of a change in the relation of the Ganges to the land which owes to that river its origin. Hence it is in the older portions of Bengal where there are dead or dying rivers that the depopulated villages are found. The most common type of malaria is benign tertian, but malignant tertian is also frequently encountered. Quartan fevers appear to be rare. The commonest malaria-carrying anopheles is *N. fuliginosus* and its larvae are found in the waters of moribund rivers, in neglected tanks, pools, borrow-pits and other water collections where weed is present. The primary cause of the depopulation is not malaria but a decay of prosperity following upon impoverishment of the soil, which no longer receives the rich silt that it used to derive from the overflow of the subsidiary channels of the Ganges. The exhaustive planting of jute has also led to soil exhaustion. Sugar-cane acts like jute but rice impoverishes the land on which it is grown but slowly.

Poverty has followed the diminution in prosperity and as a result the malarial incidence has increased. According to Bentley the remedy is to be found in improved methods of agriculture fostered by the spread of education, the extension of co-operative credit banks, and the organisation of practical demonstrations of improved methods. Engineering precautions may prevent other threatened areas sharing in the disasters which have overtaken certain districts.

A. B.

Fry (A. B.). **Malaria in Bengal.**—*Ibid.* pp. 9-10.

Malaria in the Ganges Delta is endemic but not universal. It is confined to those parts which suffered from a severe epidemic in the middle of the 19th century. Parts which then escaped are now free from endemic malaria though their general condition shows no change.

Village sanitation and adequate treatment of the sick in order to reduce gamete carriers are the measures recommended. A proper system of sanitation depends largely on education of the natives, which is urgently required.

A. B.

Hodgson (E. C.). **Malarial Survey of Imperial Delhi.**—*Ibid.* p. 11.

An account of the local conditions favouring malaria at the site of the new city. There appears to be a close relationship between the spleen-rate, depth of subsoil water and percentage of dangerous anophelines present. The malaria rate showed a very definite rise in April and May though these are not rainy months. The author thinks that this may indicate that zygotes mature only in a definite temperature and is of opinion that special attention should be paid to humidity and temperature.

[This is interesting in the light of similar recommendations as regards the life-cycle of trypanosomes in tsetse flies.]

A. B.

Graham (J. D.). **Notes on Anopheline Distribution in the United Provinces.**—*Ibid.* pp. 85-88.

Fourteen different species of Anopheles have been found in the United Provinces and a tabular statement of their distribution in the different and widely varying regions of this portion of Indian is the main feature of a paper which is chiefly of local interest.

A. B.

Stokes (T. G. N.). **Results of the Malaria Investigation in the Central Provinces.**—*Ibid.* pp. 59-60.

The question of endemic and epidemic malaria in the Central Provinces is briefly discussed. As regards the latter there is a note to the effect that scarcity of rainfall and high subsoil water are not essential to epidemic outbreaks and that the latter are not dependent on malarial endemicity. Two fatal cases of black-water fever in Europeans are recorded, one of which, however, may have been a case of malignant malaria.

A. B.

Adie (Lt.-Col. & Mrs.). **Note of an Inquiry into Malaria and Mosquitoes in the Kashmir Valley.**—*Ibid.* pp. 91-94.

The result of this enquiry was to show that in Srinagar and its neighbourhood there is no endemic malaria; there are practically no anophelines. A certain amount of imported malaria is found but the risk of spread is very slight.

A. B.

Perry (E. L.). **Malaria in the Jeypore Agency Estate.**—*Ibid.* pp. 11-13.

Major Perry thinks there is evidence to show that in the Jeypore region the stream-breeding species of anopheles, *i.e.*, *listoni, theobaldi, jeyporiensis* and *maculipalpis* are largely concerned in the transmission of quartan malaria and that the great rarity of malignant tertian, save where *culicifacies* is present, points to this mosquito being the chief vector of *P. falciparum*. [See paper by Knab reviewed in this number.] Perry believes the Jeypore estate could be greatly benefited by careful jungle-clearance operations.

A. B.

Horne (J. H.). **Malaria in the Madras Presidency. Notes on the Statistics of the Past Ten Years.**—*Ibid.* pp. 53-57.

As a result of his enquiry the author concludes that:—

1. "Only one district shows evidence of epidemic malaria: its soil is barren, its climate dry, its rainfall scanty but, when heavy, liable to cause floods. The epidemics were localised and associated with increased rainfall but not with drought in the previous year. The epidemics were followed by a marked reduction in the birth rate of the subsequent year.
2. "Normally, deaths are most frequent at the beginning and end of the year. This rise is accentuated in districts known to be malarious.
3. "Areas known to harbour endemic malaria appear to be associated with a high infantile mortality, but may possess a high birth rate."

A. B.

Rieux (J.) & Hornus (P.). **Notes sur le Paludisme dans le Maroc Occidental.**—*Arch. de Méd. et de Pharmacie Militaires.* 1913. July. Vol. 62. No. 7. pp. 1-31.

Foci of malaria are common in Western Morocco. Amongst the French troops stationed there the disease was specially prevalent in August and September 1911, and September and October 1912, but throughout the latter year it was much less in evidence than during 1911. The type was benign and the mortality low, thanks partly to this and partly to the efficiency of quinine. In every case the diagnosis was confirmed by microscopical examination. The quartan parasite was never found, benign tertian or double tertian and aestivo-autumnal being the types in evidence. Mixed or associated forms were occasionally seen. Charts are given showing the varieties of fever encountered, and the tendency of the malignant forms to lose their intermittency and become continued is duly noted. The authors accept the view that each of the three forms of the malarial parasite represents a distinct and definite species and advance arguments in favour of this view as regards the two kinds found in Morocco. The paper ends with notes on spontaneous cure and the use of quinine both as a prophylactic and as a curative agent.

A. B.

v. d. Hellen. **Notizen über Malaria bei Eingeborenen in Togo (Westafrika).** [Notes on Malaria amongst the Natives in Togo (West Africa).]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. July. Vol. 17. No. 13. p. 461.

A native assistant who accompanied the author on a journey through a malarious district for a period of over a year did not suffer from malaria until about nine months later. During these later months he resided continuously in a comparatively mosquito-free centre and did not take quinine. In this short time therefore he had lost his relative immunity. He admitted having been bitten by mosquitos while on a two days' furlough to his village and the malaria developed two or three weeks thereafter. The natives in Togo only suffer from malaria in childhood which, however, does not seem to influence the infant mortality. The latter is due to errors in nutrition. The author argues that his

demonstration of the loss of relative immunity in a native indicates that it would be unwise to carry out extensive preventive measures in a region where the possibility of the adult natives acquiring infection is only slight.

A. B.

Knab (Frederick). **The Species of Anopheles that transmits Human Malaria.**—*Amer. Jl. Trop. Diseases & Preventive Med.* 1913. July. Vol. 1. No. 1. pp. 33-43.

One of several papers forming the first number of a new journal which appears under the auspices of the American Society of Tropical Medicine. It contains no new work and is intended to indicate certain lines of research which have been neglected in the past. After criticising the new systematic nomenclature of the old genus Anopheles, the author, confining himself to the American Anopheles, tabulates the valid species with their correct names. Out of the thirty-four mentioned the following eight have been definitely proved to be malaria carriers:

albimanus.	*quadrimaculatus.*
argyritarsis.	*pseudomaculipes.*
crucians.	*pseudopunctipennis.*
intermedium.	*tarsimaculata.*

Attention is drawn to the fact that, in all probability, the same species of mosquito may behave differently towards the different species of malarial parasites, and work both in New Orleans and Formosa is cited in favour of this view. Thus *A. crucians* acts as the transmitter of aestivo-autumnal fever alone while *A. quadrimaculatus* does not convey this form but is efficient with benign tertian and quartan malaria.

An interesting subject requiring further investigation is the relation of the habits of different species of Anopheles to malaria transmission. The frequency of blood meals increases the chances for acquiring the parasites. Hence the more voracious the mosquito the more likely is it to be a carrier of infection. Again 'domestic' Anopheles are more likely to be incriminated than those classed as 'wild.' Other phases of the study of Anopheles requiring attention are the relative longevity of different species and their local distribution as governed by topographic conditions. The author advances a plea for the prosecution of these and other investigations required for the proper control of the mosquito.

A. B.

Lalor (N. P. O'Gorman). **Note upon some Unusual Forms of the Parasite of Pernicious Malaria, found at an Endemic Blackwater Fever Centre, in Blood Smears from Certain Children.**—*Indian Med. Gaz.* 1913. July. Vol. 48. No. 7. pp. 253-254.

At Wuntho in Upper Burma in the month of May the author found sporozoits in the salivary glands of a single *A. listoni* var. *albo-apicalis*. These, he thinks, were peculiar in the colouration of their cytoplasm by Leishman's stain and the arrangement of their chromatin. It is possible they may have been derived from a peculiar form of parasite which he discovered in the blood of

children in February and the earliest form of which he describes as a spore surrounded by a blue-staining envelope. These envelopes are said to rupture and the freed spores to become incorporated with the nuclei of certain large mononuclear cells, apparently of endothelial origin. Within these the spores grow. Finally each separate spore undergoes schizogony and, from each, six large spores result each of which possesses an envelope derived from the altered nucleus of the host cell. Finally these spores become free and either invade red cells, appearing as ordinary malignant plasmodia, or change into malarial crescents, which differ slightly from the ordinary gametes of *P. falciparum*. Invaded red cells are profoundly altered and the intra-corpuscular parasites have a coarser cytoplasm and are more pigmented than is usual with the ordinary parasite of malignant fever. Lalor believes them to be a different and distinct type. If so, its periodicity has yet to be determined. A coloured plate shows the sporozoits, the spores, the intra-nuclear forms(?), those found in the red cells, and the crescents.

A. B.

Clinical.

Bates (John Pelham). **A Review of a Clinical Study of Malarial Fever in Panama.**—*Jl. Trop. Med. & Hyg.* 1913. July 15. Vol. 16. No. 14. pp. 209-213.

This is a third instalment of the paper already dealt with in this *Bulletin* (Vol. 2, p. 150 and p. 221) and is concerned with malarial anaemia. The author mentions the two factors generally regarded as being operative in producing the anaemia, *i.e.*, the destruction of the red cells by the growth of malarial parasites within them, and the action of a haemolysin of unknown nature. He discards the theory of intravascular migration of parasites advanced by Rowley-Lawson* to explain the supposed inequality in the number of parasites present in the peripheral blood and the amount of anaemia following acute malarial attacks. After citing the work of various observers and especially that of Dionisi, both as regards the features of malarial anaemia and the ultimate increase which occurs in the number of red cells despite repeated febrile attacks, he gives an account of his own work. It began in 1910. Confined at first to secondary anaemias of long duration it later embraced the acute secondary anaemias following repeated attacks of primary malarial infection. The total number of cases under observation is not stated but the author groups them as follows:

1. Acute malaria cases with irregular attacks extending over a period of from two to three months—outside patients.

2. Hospital patients with a history of from five to thirteen attacks of fever extending over a period of from three to six years.

3. Cases of chronic malaria in natives who had lived amid continuous malarial infections and suffered repeatedly from fever.

In every case the number of red cells was ascertained and also the haemoglobin value either by Dare's or Sahli's method. The

* *Arch. Internal Med.* 1912. Apr. 15. Vol. 9. No. 4. pp. 420–444.

patients in the first two groups were under rather favourable general conditions, could obtain good food and were promptly treated when attacked by fever. In giving details of cases the author does not distinguish those of the first from those of the second group, but as a result of his observations concludes that where the anaemia is solely dependent on malarial infection one may expect first a sudden and marked loss both of haemoglobin and red cells. At a certain stage the losses cease and, if the attack is cured spontaneously or by treatment, a rapid rise both in red cells and haemoglobin occurs in the afebrile interval. The next attack produces a lessened effect and so on until finally the losses cease altogether. At this stage of tolerance there is a reproduction of red cells and haemoglobin in excess of the losses, that of the corpuscles usually exceeding that of the haemoglobin.

In chronic malaria on the other hand there is no tendency to improvement in the apyrexial intervals but either a stationary or progressive anaemia. Bates seeks to show that this anaemia is not due to malaria but to a concomitant uncinarial infection, or to this plus semi-starvation as a result either of lack of food or of a dietary poor in protein value and containing much coarse fibrous material. Cases with very low haemoglobin values, *i.e.*, 13 to 21 per cent. and red cell counts of from 850,000 to 1,703,000 per cubic millimetre were attributed to ankylostome infection while those with higher haemoglobin estimates seemed in the main to be due to poor food. Exhaustion of the haematopoietic organs is shown not to be operative, and the author thinks that Marchiafava and Bignami who advanced this hypothesis to explain post-malarial anaemia were dealing with cases complicated by ankylostomiasis, which is common in Italy. He is of opinion that the term malarial cachexia is misleading, serves to misdirect efforts at treatment, and ought to be abandoned in medical nomenclature. [It will be noted that Bates, beyond speaking of an unknown haemolysin, does not consider the part played by haematin in producing anaemia, a subject dealt with by Brown in a paper reviewed elsewhere in this number.]

A. B.

Marchiafava (E.). **Ueber Malaria perniciosa.**—*Deut. Med. Wochenschr.* 1913. Aug. 14. Vol. 39. No. 33. pp. 1577-1581.

After a reference to his earlier work along with Bignami the author mentions the occurrence, at the present time, of cases of pernicious malaria in the Roman Campagna. These tend to terminate fatally despite quinine treatment. He gives an account of several such cases and recalls the description of the specific parasite given by Celli and himself in 1889, together with its effect on the red cells and the changes produced by its action in the internal organs. He has found it necessary to recur to the subject because recently certain authors, *e.g.*, Deadrick, have stated that both quartan and simple tertian infections may be pernicious in type. While these forms of malaria can present severe symptoms, such as stupor, depression, prostration, &c., more especially in children and old persons, and may, in the

former, be associated with convulsions, yet these symptoms vanish quickly at the end of the febrile attack and they do not tend to a fatal issue even when treatment is delayed. Two such severe cases are cited, the one a simple, the other a double benign tertian and mention is also made of a fatal case of haemoglobinuria following quinine administration in a case of simple tertian fever. In this case there was the most severe renal inflammation the author has ever seen. At the same time he holds that pernicious malaria is a distinct entity and he lays special stress on the enlargement of the spleen in this type of malaria. The organ is not very large, its capsule is smooth, thin and transparent, and shows no evidence of a previous increase in thickness. The pulp is very soft and sometimes flows out, as it were, when the capsule is incised. The splenomegaly gives the impression of being recent and not an acute exacerbation occurring in the course of a chronic inflammation. The condition is like that found in typhoid fever save that the malarial spleen is pigmented and its pulp is softer. It is thus evident that pernicious malaria is always a recent primary infection. At the most there is only one relapse. The author thinks that a long standing malarial infection confers a certain immunity against severe malaria in comparison with what is found in those who are attacked without having suffered from a previous infection. In these latter the parasites multiply with great rapidity and are sometimes present in enormous numbers especially in the internal organs and bone-marrow. An account is given of a case in which the brain capillaries exhibited varicose extensions so crowded with parasites containing red cells that the condition was diagnosed as a true, globular stasis.

The author goes on to speak of quinine resistant strains of the parasite and of the danger of giving quinine at certain stages, as the drug may produce a precipitate sporulation leading to death as a result of injury to the nerve centres and to poisoning from the toxins set free. Sometimes when quinine has been freely given and the parasites have disappeared from the peripheral circulation death may ensue and very few parasites be found post-mortem except crescent forms, and these chiefly in the bone-marrow. In such cases there are often punctiform haemorrhages in the brain substance. When speaking of preventive measures the author advocates the establishment of hygienic stations in the malarial districts of Italy for the instruction of the agricultural labourers, &c., where quinine prophylaxis and that *prompt* treatment which is often so essential in pernicious malaria can be carried into effect. He also mentions the value of James's modification of Ross's thick film method,* though he is careful to point

* Spread a fairly large drop of blood in the form of a circle about three-quarters of an inch in diameter. Place the slide on a flat surface and allow the blood to dry. Immerse in a mixture of ten drops of commercial HCl in 50 cc. of ethyl alcohol until the haemoglobin has been dissolved out. Wash very thoroughly in running tap water for ten to twenty minutes. Dry either in the air or by blotting. Stain with Romanowsky undiluted stain for two or three minutes, then dilute freely, carrying out this dilution in successive stages, the whole process occupying about ten minutes Finally wash in tap water until no more blue colour comes from the film. For further details consult original paper in *Southern Medical Journal.* Vol. 4. 1911. p. 698. The above summary, however, gives the essentials of the method.—A. B.

out that it is not suitable for those who are tyros in the examination of blood films for the diagnosis of malaria.

A. B.

Acton (H. W.) & Knowles (R.). **Latent Malaria.**—*Proceedings of the Third Meeting of the General Malaria Committee held at Madras.* Nov. 18, 19, 20, 1912. pp. 22-23. (1913. Simla: Govt. Central Branch Press.)

This is an account of work undertaken to give greater precision to the present method of diagnosing latent malaria. The first part deals with the definition of latency and sub-divides latency into distinct phases, such as the latency of the incubation period, that preceding recrudescence and that preceding relapses, these latter two being differentiated. The authors believe in parthenogenesis as one of the factors concerned in relapse. Two indirect tests for latent malaria are employed:—(*a*) The urinary urobilin test; (*b*) The leucocyte count.

The following summary sufficiently explains their views:—

1. "The presence of urobilin in the urine in large quantities indicates that haemoglobin is being destroyed. The blood destruction, except in certain well defined diseases, is due to destruction of erythrocytes by malarial parasites. If there is no fever present the patient is in the latent stage of the disease.
2. "In the latent period of relapse the asexual cycle is absent in the peripheral blood and gamete formation is occurring. The urobilin consequently is diminished in amount, unless the functions of the liver are impaired in which case urobilin may be increased.
3. "The absence of urobilin from the urine indicates either that blood destruction is not occurring or that the liver is still able to deal with the products of haemoglobin destruction. In such cases other tests for latent malaria must be applied.
4. "A leucopenia of 2,000 to 7,000 per c.mm., or a leucocytosis, 16,000 or more, in the absence of other causes, is suggestive of latent malaria.
5. "A high relative mononuclear percentage is also suggestive that protozoal parasites are present.
6. "A fluctuating leucocyte count with a high mononuclear percentage at the leucopenic stage is very suggestive that malarial parasites are still present somewhere in the body.
7. "The increase in the total mononuclear and hyaline cells is not a real but an apparent one, due to fluctuations in the number of the polymorphonuclear leucocytes."

Tables and charts are mentioned but have not been reproduced.

A. B.

Henson (Graham E.). **The Diagnosis of Malaria.**—*Southern Med. Jl.* 1913. July 1. Vol. 6. No. 7. pp. 423-426.

A plea for laboratory diagnosis in suspected malaria and a suggestion that an effort should always be made to take blood smears for diagnosis at a time when it is probable that the parasites are in greatest profusion in the peripheral blood. In benign tertian infections this is from four to six hours after the chill and thereafter to within six hours of anticipated sporulation. In quartan the parasite is more easy of detection throughout the entire cycle and hence the timing of a smear is not so important. In aestivo-autumnal types two hours after the chill or exacerbation and thereafter for two or three hours will be found the most

likely periods. When, however, crescents have formed they may be found at any time. In a discussion which followed the reading of the paper Bass of New Orleans stated that there never occurs a time when there are not enough parasites in the blood of a patient who is having chills and fever from malaria but that the parasites can be found. The proper time to take blood therefore is whenever one sees the patient for diagnosis. [While the latter part of the statement is no doubt true, Henson's recommendations are likely to be helpful especially to those with little experience in blood examination or little leisure to conduct it in a searching manner]. A diagnosis is apt to be specially difficult if quinine has been administered. In such a case a tentative diagnosis of malaria may be made when:—

(*a*) A clinical history of malaria is obtainable.
(*b*) The patient has an enlarged spleen.
(*c*) A leucopenia is present.
(*d*) The red cell count is below normal.
(*e*) The haemoglobin is reduced.
(*f*) A differential count shows an increase of large mononuclears.

A. B.

Freeman (James V.). **The Incidence of Malaria in the Puerperium.** —*Southern Med. Jl.* 1913. July 1. Vol. 6. No. 7. pp. 429-430.

The author insists on the importance of distinguishing between malaria and sepsis in the puerperium. Malarial infection in childbed produces a fever within the first week without definite chill. Unless the patient is known to be a malarial subject, it can only be diagnosed by blood examination. This, together with absence of the usual signs of sepsis, febrile periodicity and the application of the therapeutic tests, enable a diagnosis of malaria to be established. As was pointed out in a discussion on the paper the mere presence of malarial parasites in the peripheral blood does not always justify one in assuming that malaria is the sole cause or indeed even a cause of the febrile condition.

A. B.

Kahn (Ida). **Some Experiences with the Subtertian Fever in Kiangsi.**—*China Med. Jl.* 1913. July. Vol. 27. No. 4. pp. 231-236.

In Kiangsi subtertian malaria causes a greater mortality than tuberculosis and no age is exempt from its attacks, which are sometimes of lightning-like rapidity. The bilious form is very common and a severe case successfully treated by intramuscular injections of quinine bi-hydrochloride and stimulants is recorded. The algide type is not so frequent but a form of malarial broncho-pneumonia in children is far from rare. If sufficient quinine is not given, the lung symptoms will not quickly subside and yet if the quinine is pushed there is danger of amblyopia, as in a

case described by the author. Here, however, the quinine was continued, but given at longer intervals, and the sight was rapidly recovered and later appeared to be quite normal.

A. B.

Woolley (J. M.). **Malaria in the Andamans: Fever with Jaundice Cases.**—*Indian Med. Gaz.* 1913. July. Vol. 48. No. 7. pp. 266-267.

This is an account of a peculiar "Fever with Jaundice" which has been noticed in the Andaman Islands during the past three or four years. Hitherto it has been considered malarial but the writer thinks it may yet have to be classed as a distinct entity. The jaundice appears on the third or fourth day of the illness and is often intense. In bad cases there are petechial haemorrhages in the skin and bleedings from the gums, delirium and a feeble and rapid pulse. Forty per cent. of the cases die, usually from cardiac syncope. The post mortem appearances are summarised but are not specially characteristic.

Malarial parasites are not found in the blood but in fresh blood-films small rod-like, or round, non-pigmented, motile bodies, have been seen. They cannot be stained but the author thinks they are parasites and cause the disease. [They are probably merely artefacts, the so-called "Maraglianos"]. The treatment of this fever is entirely symptomatic. Quinine is of no avail.

A. B.

Treatment.

MacGilchrist (A. C.). i. **Pharmacological Action and Uses of Quinine.**—*Proceedings of the Third Meeting of the General Malaria Committee held at Madras*, Nov. 18, 19, 20, 1912. pp. 17-18. (1913. Simla: Govt. Central Branch Press.)

ii. **Intravenous Injections and Subcutaneous Infusions of Quinine Salt Solution.**—*Ibid.* p. 97.

i. The author believes in large doses of quinine if treatment is to be efficient. Such doses taken with or soon after meals at eight-hourly intervals keep the concentration of quinine in the blood at a high point throughout the twenty-four hours. There are no objections to giving quinine during the fever period. As regards prophylaxis it is stated that fifteen grains of quinine taken on two consecutive days each week keep the malarial parasites in subjection as long as such treatment is in force, but it does not disinfect the patients. Relapses may occur when the prophylactic treatment is stopped but such treatment does not tend to increase the liability to, or the occurrence of relapses after its cessation. Little definite is known regarding the action of quinine on the blood vessels, but its action on the uterus under different conditions has been noted. It will greatly increase the expulsive contractions of the already active pregnant uterus but cannot induce or originate expulsive contractions in the quiescent pregnant uterus. The action of quinine as a local anaesthetic practically amounts to a chemical resection of the nerves. The author concludes with a plea for a more extended

use of quinine base in a pure precipitated amorphous form. Its advantages are:—

1. Sparing solubility.
2. Comparative tastelessness.
3. Absorption as quick as with a salt.
4. Bulk and weight small.
5. Non-haemolytic action.
6. Cheapness.

Quinine base can be administered intravenously in two ways:—

(*a*) As a 1 in 135 solution in 33 per cent. alcohol in saline.

(*b*) As a 1 in 2,000 or 5,000 solution in saline.

ii. The author states that, although in a previous paper* he gave 1 in 150 as the strongest solution of a quinine salt which could safely be introduced intravenously without danger of thrombosis, he did not recommend the use of solutions of this concentration as they are very irritating. As he mentioned, seven grains or so of quinine bi-hydrochloride should be dissolved in two or three pints of normal saline. He refers to the new method of James, *i.e.*, subcutaneous infusions [see this *Bulletin*, Vol. 2, pp. 151-152], and thinks it must cause extensive local disintegration of the tissues at the seat of the infusions, owing to the concentration of the solution used.

[James's method has been used in several cases in the Anglo-Egyptian Sudan with excellent results and no untoward effects.]

A. B.

Justi (Karl). **Zur Methodik der Chinindarreichung bei Malaria.** [On the Methods of Quinine Administration in Malaria.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. Aug. Vol. 17. No. 15. pp. 505-522.

This paper is largely a compilation and criticism of the views of various authors as to the best way of administering quinine in malaria. The author enters very fully into the matter and, in discussing the oral methods as compared with injections, considers the pharmacological and clinical data on which a conclusion as regards their respective merits must be based. He is apparently unacquainted with some of the recent Indian work on the subject and confines himself in the main to that of German observers. At the same time he has had an extensive experience at Hongkong, extending over 25 years, and he carefully explains the reasons which have led him to adopt the procedure he now follows and which he recounts in detail.

He agrees with Werner of Hamburg that, in oral administration, Nocht's method of fractional doses, *i.e.*, 0·2 grammes every two hours from 7 a.m. to 3 p.m. daily is better than a single, large dose, *i.e.*, one gramme, as it causes less vomiting, and the sickness, if it occurs, is less severe. He finds that Werner's intravenous injection of 1½ grammes of quinine urethane in 200 c.c. of physiological salt solution, as employed

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* *Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India* (New Series). No. 41. 1911.

in severe comatose cases, is better suited for hospital than for private practice as it presents technical difficulties and must infallibly lead to delay if used where the necessary apparatus cannot always be kept ready at hand. He does not agree with WERNER'S conclusions as to the comparative inefficacy of intramuscular injections and believes that WERNER'S views on this method were based on a misconception of the action of quinine, so administered, on the malarial parasites.

As he says, the objections to the ordinary injection methods, subcutaneous and intramuscular, are that the quinine is supposed to be less active than when given by the mouth and that there are apt to be unpleasant sequelae in the way of pain, local necrosis and suppuration. He discusses these objections in the light of what is known regarding the pharmacological action of the drug, admitting that we are still in the dark as to some of its effects and the changes it undergoes in the body. Various authors are quoted to show that both in subcutaneous and intramuscular injection this destruction and retention of quinine in the tissues, &c., is as great as when it is given *per os*. If, as MARIANI holds, and he is supported by GIEMSA and SCHAUMANN, the amount of quinine excreted by the kidneys is proportional to its anti-parasitic power, then we must conclude that the injection method has only half the value of the oral. ZIEMANN, however, is of opinion that it is not the eliminated quinine but that used up by the body, *i.e.*, united to cell protoplasm, which plays the chief part in the therapeutic action. That the matter is not so simple is indicated by the recent researches of PLEHN and GROSSER who have shown the special rôle played by the endothelial cells of the vessel walls in rapidly removing quinine from the circulating blood. A similar selective action on the drug is in all probability exerted by the malarial parasites themselves. PLEHN believes their destruction takes place in the circulating blood and not in the internal organs (GIEMSA and SCHAUMANN).

After a further consideration of the experimental work, both of the authors already mentioned and that of ARNAUD, Justi decides that the data available do not support the objection which has been raised on pharmacological grounds to the employment of the injection methods. He then passes to a consideration of the objection advanced on clinical grounds and is here able to speak with considerable authority as he has had experience of nearly 2,000 injections. In only three cases did abscesses result and these, for reasons stated by the author, cannot fairly be considered as failures. In dealing with the question of tissue destruction he gives the details of his aseptic technique on which so much depends. Here there is nothing special to note but he lays great stress on the choice of the place where the injection should be made. This, according to his view, is the gluteal region and only the gluteal region, both in the case of male and female patients. The neighbourhood of the sciatic nerve is to be avoided and he is strongly opposed to mere subcutaneous injection. [Apparently he is not familiar with the modified method introduced by JAMES in Panama (see this *Bulletin*, Vol. 2, pp. 151-152).]

Provided the precautions mentioned are adopted there is no objection to a daily injection. Observations are recorded showing the efficacy of the injection method as regards its effects on the parasites (benign tertian and malignant), on all three types of fevers, and on the enlarged spleen both in acute and chronic cases of malaria. For details the original paper must be consulted but it may be said that the author finds that, as far as the disappearances of ring forms and older schizonts is concerned, the intramuscular injection is just as rapid in its effect as the oral administration while, possibly, its action is superior in the case of gametes. In a brief summary he says that subcutaneous injections are not to be recommended, that intramuscular administration is quite as useful as oral administration and may be used in preference to Nocht's methods in case of sickness and vomiting, and even in those exhibiting somnolence and coma so long as intravenous injection is not imperatively indicated.

In his own practice the author begins with one injection repeated every 24 hours and continued for some time after all parasites have disappeared. In pernicious cases never less than six injections are given. He then exhibits quinine by the mouth, one gramme on each of two successive days, usually Saturday and Sunday, *i.e.*, about 30 grains in the course of a week. In suitable cases, however, he employs Nocht's method from the beginning, reverting to the injection if sickness and vomiting supervene.

A. B.

Waters (E. E.). **The Pure Amorphous Alkaloid (of Cinchona).** [Correspondence.]—*Indian Med. Gaz.* 1913. July. Vol. 48. No. 7. p. 285. **The Amorphous Alkaloid of Cinchona.** [Editorial.]—*Ibid.* pp. 273-274.

Major Waters writes to explain the nature of the pure amorphous alkaloid of cinchona previously described by him [see this *Bulletin*, Vol. 1, p. 650]. It is a sticky, treacle-like substance which, owing to its peculiar physical characteristics, is difficult to incorporate in large doses in tablet form. So far one and two grain tablets only have been issued. Confusion has arisen because in addition to this *pure amorphous alkaloid* there is the amorphous cinchona alkaloid. This is only 40 per cent. of the strength of the pure alkaloid, from which it differs physically, and hence can be issued in 3 1/3 grain tablets. To prevent confusion Waters suggests the name "Laverain" (after Laveran) for the pure amorphous alkaloid, which is a very complex body. The Editor of the *Indian Medical Gazette* points out that as Quinoidine is the old name for this drug it must remain in force.

As a result of Major Waters' letter the *Indian Medical Gazette* has an editoral on the subject which mentions both these alkaloids under the names of Quinoidine and Residual Alkaloid respectively. It points out that as the dose of the former is small, a three grain tablet containing a one grain dose, is quite satisfactory. The Government Quinologist furnishes a useful general note on "The Amorphous Alkaloid of Cinchona Bark" which should be consulted by all interested in the subject. Residual

alkaloid is really an amorphous mixture of *all* the alkaloids of cinchona bark, having an average composition of:—

Quinine	3
Cinchonidine	2
Quinidine	20
Cinchonine	35
Quinoidine	30
Water, Ash, &c.	10
	100

The effect of the mixture is not due to any one alkaloid alone, for all are effective in the cure of malaria while it is supposed that the amorphous state of the preparation renders it more readily assimilated.

Quinoidine in the form of its salts can be separated out owing to their greater solubility. Some traces of the other alkaloids remain in the product finally obtained, which is evidently a mixture of substances as it varies in consistency according to the kind of bark from which it has been derived. At present it is being prepared in India from Residual Alkaloid, but it may be necessary to select and grow strains of cinchonas giving a larger yield of this particular alkaloid.

A. B.

Muir (E.). **The Diagnosis and Treatment of Chronic Malaria and Kala-azar.**—*Indian Med. Gaz.* 1913. July. Vol. 48. No. 7. pp. 267-268.

The author has extended his kala azar treatment (see *Kala Azar Bulletin*, 1912, July, No. 3, 125-126) to cases of chronic malaria but he has modified it so that, instead of giving hypodermic or intra-muscular injections of a very strong acid solution of quinine sulphate, he now relies on the following mixture to produce the local irritation which he believes confers the benefit:—

	Drachms.
Turpentine	1
Camphor	1
Creosote	1
Sterilised olive oil	$2\frac{1}{2}$

The camphor and creosote are mixed first and then the turpentine and oil added. 5-15 minims are injected into the muscles on both sides of the body, the latissimus dorsi or glutei being the most suitable sites. There is little pain at the time of the injection but pain and swelling come on later proportionate to the amount injected and to the susceptibility of the patient. In chronic malaria the reaction is more marked than in kala azar. One or two injections in moderate cases and up to fifteen or twenty injections given weekly in more advanced cases restore the patient to a marvellous degree of health and strength.

A. B.

Kopylow (N. W.). **Ueber Splenektomie bei Malaria-affektion der Milz.** [Splenectomy in Malarial Affections of the Spleen.]—*Arch. f. klinische Chirurgie.* 1913. June 17. Vol. 101. No. 3. pp. 708-734. With 6 text-figs.

This paper opens with an interesting historical account of the operation for removal of the spleen which, as far as chronic malaria is concerned, was first performed by Küehler in 1855. The patient died, but shortly afterwards Dorsay operated successfully in a similar case. The author describes the changes induced in the spleen by chronic malaria and the functional disturbances produced by the enlarged and altered spleen in neighbouring organs. He also deals with the subject of "floating spleen," which is most common in women.

Splenectomy is indicated for malarial affections of the spleen—

"1. In splenic rupture and torsion of the pedicle, the latter tending to occur in floating spleen and causing symptoms of peritonitis. In these cases the operation appears to be vitally indicated and must be performed at once, otherwise death will undoubtedly occur.

"2. In cases of enlarged movable spleen—floating spleen. It is relatively easy to perform the operation here; nevertheless pedicular torsion with all its severe sequelae must always be anticipated.

"3. In cases of large, immovable, painful spleen, in which medical treatment has given no noticeable result."

Although in cases of slight hypertrophy of the liver, moderate cachexia and advanced age the mortality percentage is still fairly high (about 30 per cent.), the operation is justifiable; but it is contra-indicated

"1. When there is considerable cachexia with hyperaemia and marked diminution of the haemoglobin content (below 40 per cent.).

"2. When there is severe atrophic cirrhosis.

"3. When the general condition is bad with diseased digestive and uro-genital organs.

"4. When there are very extensive adhesions, especially to the stomach and diaphragm."

The author gives a careful account of 13 splenectomies performed in the Balachnin Hospital of the Naphtha works, close to Baku in the Caucasus. Ten of these were his own operation cases and nearly all the patients belonged to the peasant class.

Attacks of malaria were observed in three patients during their stay in hospital after operation. Other complications and sequelae are mentioned. There follows a valuable section dealing with the operative technique, considered under the following headings, (*a*) Section through the abdominal wall, (*b*) Ligature of the pedicle, (*c*) Separation of the adhesions, (*d*) Closure of the abdominal cavity.

Death after splenectomy is stated as being due to shock, haemorrhage, peritonitis, pneumonia, gangrene of the walls of the stomach and intestine, or as the result of malarial changes in the liver and spleen.

A mortality table compiled from various sources is given, from which it appears that the mortality ranges between 7 and 60 per cent. In Kopylow's own cases it was 23 per cent., or, excluding a case operated on *in extremis*, 16 per cent.

When successful the operation gives good results, the patients being able to resume their work. The author thinks there is a distinct future for splenectomy in malarial affections of the spleen, but he is careful to point out that the technique must be improved and care taken to follow correct indications for operative interference.

Five of the six figures illustrating this useful paper are photographs of spleens removed by the author.

A. B.

DEGORCE (A.). **Accès Palustres Mortels ou Tenaces observés après la Splénectomie.**—*Bull. Soc. Méd.-Chirurg. de l'Indochine.* 1913. June. Vol. 4. No. 6. pp. 299-306.

An account of three cases showing that splenectomy may be followed by fatal or very severe attacks of malaria. In two of the cases death resulted and was undoubtedly due to the operation, which was not in any way complicated and did not occupy an unduly long time. There was no doubt that the surgical procedure was to blame and energetic treatment with quinine failed to save the patient. The third case was an example of a severe malarial attack occurring fifteen days after splenectomy and characterised by a fever very resistant to quinine given both by injection and by the mouth. The author discusses the cause of these accidents.

Traumatism might explain the first two cases where the attacks quickly followed the operation, but he is more inclined to believe, a belief strengthened by the history of the third case, that the extirpation of the spleen interfered with the defensive mechanism of the organism. He concludes, therefore, that splenectomy is only justifiable in those cases where the splenomegaly results in much suffering and where the least injury is apt to cause rupture of the spleen. When splenectomy is decided upon, even if no parasites can be found in the peripheral blood, it is advisable before operation to treat the patient thoroughly by a series of quinine injections.

A. B.

PROPHYLAXIS.

LEGENDRE (J.). **Prophylaxie du Paludisme en Italie.**—*Bull. Soc. Path. Exot.* 1913. June. Vol. 6. No. 6. pp. 468-476.

To TERNI belongs the credit of being the first in Italy to suggest the utilisation of fish for the destruction of mosquito larvae. The fish he recommended were carp, tench and eels, which not only possess a hygienic value but are of economic importance and have thus an advantage over "millions" and other small species of fish which are only of use as destroyers of larvae. TERNI examined the stomach contents of small tench taken from the water in rice cultivations and found 60 to 80 larvae of anophelines and other mosquitos in each of them. The author

gives an account of the systematic pisciculture now conducted in the rice-growing areas of Lombardy. Carp are employed, being introduced as young fry which, thanks to abundant food, rapidly increase in size and weight. During the winter they are kept in a special basin and fed with kitchen scraps. In the summer they are reintroduced into the water of the rice fields. After their second season in the rice fields the carp at the age of 16 months are eaten or sold at a good profit. The rice culture benefits from their presence as less weeding (a costly operation) has to be done and it is found that in the carp-stocked cultivations the yield of rice is equal or even superior to that elsewhere. There is no doubt that from the mere economic standpoint the pisciculture is a great success and it is being adopted with enthusiasm throughout Lombardy, the species of carp employed being *Cyprinus carpio* var. *specularis*, which is obtained from Germany. Sufficient evidence has not yet been accumulated to permit a definite statement being made as regards the anti-malarial value of this measure but there is enough to show that it is really beneficial and likely to have a future. The author recommends the adoption of pisciculture in Madagascar and Indo-China.

The paper then considers other anti-malarial measures employed in Italy: quininisation, hydraulic works and mechanical protection. The so-called "quinine preventive" method of Celli, the pre-epidemic cure of Golgi and the plan followed by Terni receive brief mention. The last mentioned consist of an intramuscular injection of the following formula:—

	Grammes.
Basic chlorhydrate of quinine	3
Ethylurethane	2
Oil of vaseline	5

Emulsify by heat.

In heavily infected localities the injection is repeated once a month and this method is recommended for use in the Colonies and in countries where it is impossible to establish a regular daily quininisation.

A. B.

Celli (A.). **Malaria in Italy during 1910.** [Translated from the Original by Major N. P. O'Gorman Lalor. With a Preface by the Translator.]—*Proceedings of the Third Meeting of the General Malaria Committee held at Madras*, Nov. 18, 19, 20, 1912. pp. 113-150. (1913. Simla Govt. Central Branch Press.)

The translator summarises the conclusions of Celli as set forth in this long report as follows:—

1. "That quinine taken at an approximate daily rate of three grains in the morning and three at night, throughout the fever season by a healthy individual in a severely stricken malarial locality, practically guarantees him against the risk of malarial infection.
2. "That quinine similarly consumed by every individual, whether presumably healthy or malarially suspect, in a malarial community, affords similar and proportional guarantee as regards the community.

3. "That quinine taken in the prophylactic quantity mentioned, is absolutely devoid of harmful effect, proximate or remote, to the consumer.

4. "That the risks to which subjects of chronic malarial infection are said to be exposed by daily quinine consumption, viz.:—

"(*a*) Intracorporeal development of haemamoebic types resistant to quinine (*chininfasten* Malaria Parasiten) and

"(*b*) Quinine haemoglobinuria,

are assuming smaller and smaller proportions with our increase of knowledge, and are probably non-existent when quinine is taken with perfect regularity.

5. "That there is at present but one preparation of quinine suitable for administration to young children—the tannate—and that it is best administered made into a sweetmeat with chocolate. (This latter suggestion unfortunately cannot be utilised under Indian climatic conditions.)"

The report itself is divided into two portions; Part I. dealing with epidemiology and Part II., which is much the larger, setting forth Celli's views on prophylaxis.

Some paragraphs in Part I. are devoted to the question of agriculture and malaria and Celli states that "more rational cultivation in marshy localities limits or reduces anophelic influence only in part, and though it proves beneficial—whether because of better nutrition arising from more abundant and varied products of the soil or because of the possession of house and clothing, with a less precarious mode of life—it fails notwithstanding by such indirect means to preserve man from malaria unless prompt and immediate medical, especially quinine prophylaxis, comes to the rescue."

It has been found that, whereas in Sardinia miners are more affected than agricultural labourers, the reverse is true in Sicily. This may be so because the lead poisoning to which the Sardinian miners are more or less subject predisposes them to malaria. Some of Celli's own conclusions terminating Part II. may be quoted. He says:—

(*a.*) "Since we have as yet no prompt and certain means of diagnosing latent infection, those parasitic forms which subserve the conservation of species in man and mosquito (manage to survive and) are still . . . . absolutely resistant to quinine and every other remedy. No remedy therefore, quinine not excepted, is always effective . . . and so not even with the most accurate inter-epidemic and pre-epidemic treatment . . . can we believe it possible for malaria to be exterminated in an extensive locality already overrun by the disease.

(*b.*) "The *Consensus Omnium* to-day places quinine prophylaxis in the first rank amongst anti-malarial measures not alone for civilized countries but even for the colonies.

(*c.*) "In our more intensively cultivated levels, no less than in those under broad cultivation, the anti-anophelic campaign (except by the protection of the houses of a few of the better off against mosquitos) is not practically feasible. Mixed prophylaxis (anti-plasmodic and anti-anophelic) on the other hand, where . . . it can be simultaneously carried out by the administration of quinine and the provision of wire gauze netting to keep mosquitos at a distance from dwellings, conduces to reduce malaria to a minimum and to render it as mild as can possibly be wished."

The other conclusions chiefly concern Italy but there are many interesting facts in the report, which is well furnished with statistics and which points to the good results achieved by the quinine methods in Cochin China, Algiers, Greece (Anchiolos) and amongst the personnel of the German Navy.

A. B.

Celli (A.). **Die Malariaabnahme in Italien.** [Decrease of Malaria in Italy.]—*Zeitschr. f. Hyg. u. Infektionskr.* 1913. July 17. Vol. 75. No. 1. pp. 123-146.

Celli begins his lengthy review with a brief historical account of the Roman Campagna and the malign influence which malaria has had upon it and its inhabitants. He then describes what has been accomplished at Cervelletta, the estate in the Campagna where the great anti-malarial campaign began. Personal and general mechanical prophylaxis was found to be impossible in the case of the peasants while efforts directed against mosquitoes were only partially successful as, indeed, the author holds they must be throughout Italy. It was not till systematic quininisation was adopted that real progress was made. He goes on to speak of the malaria research stations throughout Italy and considers malaria in that country from an epidemiological standpoint. Latent infection carriers are found amongst both children and adults and, despite the most careful treatment, children relapse in the proportion of 38 per cent. and adults of 51 to 52 per cent. Childhood therefore is not specially predisposed to relapse.

For the general reader the section dealing with the research work by Gaglio and his pupils as regards quinine will be found the most interesting and instructive part of the paper. Much that is stated is now well known but there are certain facts which merit attention. Thus it is noted that quinine hydrate or water-free quinine or the combinations which are insoluble in water, *e.g.*, the tannates, are absorbed just as well as the salts which are soluble in water. Again, although quinine is absorbed in the ordinary way, entering into a slight combination with hydrochloric acid in the stomach, a more important combination is with the bile acids and the carbon dioxide of the intestinal canal. So far as absorption goes it is immaterial whether the stomach is full or empty. Daily doses of quinine (medium — 30 to 40 centigrams) [roughly 5½ to 6 grains] can be tolerated longer and better than was at first believed. The singing in the ears ceases after the first two or three days and it has been found that the drug, if properly given, is harmless and even aids nutrition.

Tolerance is readily established and quinine can be discontinued without any unpleasant results, while the fact of the organism being used to small or moderate doses in no way inhibits the action of curative doses, if these have to be given. It has been found that after the lapse of three days no quinine is to be detected in the urine, no matter what preparation is used or how it is given, and, as after a pause of more than three days in the administration, the disturbances which quinine causes again show themselves, it is better to give it daily or at least every second or third day. The salts which are insoluble in water are best tolerated because they are absorbed more slowly. The organotropic action of quinine, especially in sensitive individuals or those suffering from an idiosyncrasy or a tendency to black-water fever, is very restricted and ceases altogether if it is given in colloidal combination with tannic acid (so-called tannate), or with certain lipoids (lecithin, cholesterin). The tannate has been found better than the ethyl carbonate (euquinine) and di-quinine

carbonate (acistochrina) [? aristochinin], because these latter forms are always bitter and it is not easy to prepare them in a pleasant form, such as chocolate pastilles and the like. The tannate is also the least toxic of all the quinine salts and is especially useful in the case of children and in persons suffering from gastric and intestinal disturbances. The muriate and the bi-muriate are the best salts for general use.

The prophylactic method, employed first at Cervelletta, was to give throughout the summer and autumn two tablets (40 cgm.) daily to adults, one tablet to older children and a chocolate tablet with an appropriate dose to the smaller children. A great change resulted which was wholly attributable, according to Celli, to the quininisation. He passes on to deal with the special legislation now in force regarding malaria and the sale of quinine, and furnishes numerous statistical tables to prove the value of the quinine method. The article concludes with an account of the laws for improving hydraulic works (drainage of swamps, proper irrigation, clearing of canals, &c.) and of the statutes governing land improvement and settlement.

A. B.

Bentley (C. A.). **Quinine Propaganda.**—*Proceedings of the Third Meeting of the General Malaria Committee held at Madras*, Nov. 18, 19, 20, 1912. pp. 99-104. (1913. Simla: Govt. Central Branch Press.)

Although India consumes at present about one-sixth of the world's supply (17,000,000 ounces annually) of quinine, the vast proportion of her malarial stricken population receives no benefit from the drug. Much that is consumed is wasted owing to professional and lay ignorance while the existing methods of distribution have proved, more or less, failures. A system similar to that employed in Italy should be adopted, the widely advertised quinine being sold at a small profit and the revenue derived from the sale devoted to grants of quinine to dispensaries, &c.

The author believes the simplest curative method to be the administration of 20 grains a day for three weeks, in tablet form so long as the tablet is readily friable. Two sizes of bottles (the bottles being priced) should be adopted for general public use, one labelled "complete treatment" containing 126 $3\frac{1}{3}$ grain tablets, the other marked "relief treatment" holding 30 similar tablets. Full directions should be given as to dosage and the wrapper should contain a short history of quinine and an account of malaria. In conclusion the author urges an increase in cinchona plantations in India.

A. B.

Graham (J. D.). **School Quininisation Experiments in the United Provinces.**—*Ibid.* pp. 105-111.

A record of the benefits which have resulted from a systematic quininisation both of teachers and scholars in schools throughout the United Provinces. Details as regards dosage and cost are given. In the case of children the author found no difficulty in administering uncoated tablets of quinine of from one-half to 5 grains. There was no compulsory administration.

A. B.

Turner (J. A.). **Malarial Operations in the City of Bombay.**—*Ibid.* pp. 151-176.

Bombay, a city of 979,445 inhabitants and with, in addition, a large floating population, a total area of 22·53 square miles and an average annual rainfall of 72 inches was visited by a severe epidemic of malaria in 1908. As a result of a report on this outbreak by Bentley a special malaria officer was appointed and now the Medical Officer of Health reports on the methods which have been adopted to combat the disease and the difficulties which have been encountered in doing so.

The former have been very thorough. The Anophelines of Bombay are *A. rossii, barbirostris, listoni, stephensi, jamesii, culicifacies* and *fuliginosus.* With the exception of *A. rossii* all convey malaria. Attention however has not been confined to the mosquito aspect of the question as the following list of measures taken will demonstrate:—

1. Closing of wells and cisterns breeding larvae.
2. Treatment of all temporary pools and puddles with pesterine.
3. Giving a trial to fish before taking legal steps.
4. Distribution of quinine.
5. Filling in all hollows and low grounds with a view to remove potential sources of mosquito-breeding and to improve sanitation generally.
6. Improving of drains and gullies and extension of drainage schemes.
7. Improving of the general conservancy of the city.
8. Teaching the public by handbills and lectures with magic lantern slides.
9. Taking action in Court where parties defy the Municipality.
10. The spleen census of children and the examinations of blood of patients attending dispensaries.
11. A weekly return of cases of fever from all private and public dispensaries.
12. The examination of all species of mosquitoes found at different times of the year.
13. Proposed scheme for filling in a portion of foreshore and reclaiming another portion.

The difficulties in such a campaign are naturally very great. Details are given regarding the methods employed. With reference to well covers the author states that two kinds are allowed. One type is made of wire gauze, 20 meshes to a running inch. It is covered by expanded metal in order to protect the gauze underneath. With this sort of cover a trap door under lock and key or a hand pump is allowed if the water is required for religious observances, washing and similar purposes. These covers cannot last long on wells in open compounds as the force of the monsoon rains is apt to break the gauze which is also liable to rust. Hence there is a second type where the well is covered in with brick and cement except for a small opening of from 1½ to 2 square feet guarded by a trap door either of wire gauze or wood. These trap doors have to be kept under lock and key and opened only when water is actually being drawn. A leaflet giving hints for the prevention of malarial fevers is reproduced.

[The hints are excellent but the statement under No. 5 to the effect that "the well should be protected by a close fitting cover,"

would be improved by the addition of the words "and such covers must be frequently inspected and kept in good repair to the satisfaction of the sanitary inspector."]

A. B.

Graham (J. D.). **Progress of present Anti-Malarial Schemes in the United Provinces.**—*Ibid.* pp. 177-182. With 3 maps.

The towns of Nagina, Saharanpur and Kosi in the United Provinces having been malarially surveyed and reported upon were inspected by special committees in May 1912. A report and estimate were furnished and then the Irrigation Department prepared detailed estimates of their projects. This was necessary as the Nagina project deals chiefly with tanks, water-logging and wet cultivation, the Saharanpur project with defects due to over-irrigation by canals, water-logging and wet cultivation and the Kosi project with irrigation, deficient drainage and water-logging.

Briefly the measures employed consisted in the abolition of rice cultivation within half a mile of the site dealt with, the limiting of canal irrigation, the flushing of canals, the altering of canal levels, the water-proofing of canal beds, the filling in of tanks and the regulation of borrow-pits.

[The report must be consulted for details, but it is a useful one for in the past it has not been easy to obtain the kind of particulars which it presents and in many countries irrigation works and anti-malarial campaigns are closely associated].

A. B.

Balfour (Andrew). **A Year's Anti-Malarial Work at Khartoum.**—*Jl. Trop. Med. & Hyg.* 1913. Aug. 1. Vol. 16. No. 15. pp. 225-232. With 5 figs. and 1 map.

Few papers dealing with the epidemiological aspects of malaria in Africa have appeared recently, so the author believes it may be of interest to give an account of the anti-malarial work in Khartoum for the year 1912. This year was an especially interesting one because the conditions favoured a prevalence of malaria, and Khartoum, which has enjoyed a very considerable immunity in past years from the disease, did not altogether escape, having been visited by a small epidemic following the occurrence of a short but heavy rainfall. This may have been due to the fact that very little attention has been paid, until recently, to the irrigated areas along the Nile to the North and far outside the municipal boundaries. These areas having gone from bad to worse began to constitute themselves a nuisance as nurseries for anophelines.

The local conditions of Khartoum, as regards malaria and mosquitoes, have already been considered fully by the author and they are therefore not specially dealt with again here. As regards the population a census was taken in the course of the year and the following are the official figures for the civil popula-

tion of Khartoum and Khartoum North, over which the Sanitary Service exercises control:—

Khartoum City and Adjoining Villages.	
Europeans	1,114
Egyptians and other non-Europeans..	8,645
Natives	15,963
Total	25,722
Khartoum North.	
Europeans	482
Egyptians and other non-Europeans..	1,467
Natives	15,176
Total	17,125
Central Prison (average)	363
Grand total for civil population ...	43,210

In addition the British and Egyptian Army garrisons amount to 5,507 men, 780 of these being British troops.

A series of tables give meteorological statistics for 1912, details of rainfall at Khartoum for August 1912, mosquito statistics for 1912 in Khartoum and Khartoum North, and anopheline infestations where pupae or pupal shells were found in the same year. A very excellent map gives a plan of the town with the areas where malaria has broken out and their relationship to mosquitoes, while photographs illustrative of anopheline breeding pools and mosquito traps are added. 87 cases of locally acquired primary malaria were notified throughout the year; a table shows the monthly distribution of these cases; 62 occurred in Khartoum and 25 in Khartoum North. There were no deaths amongst those attacked, the only fatal case recorded having acquired his infection outside Khartoum. Possibly some cases occurred amongst the native population but were never returned. A series of cases in December was rather interesting. These occurred amongst British troops and a most careful search, with the free use of traps, failed to reveal any anopheline infection of the barracks. Further, the anopheline infested area at Buri had been put out of bounds, while there was nothing to show that infection had been derived when the men were in camp on the main Nile. The most possible explanation was that they were recrudescences of slight or masked cases, relapses taking place as the cold weather set in.

It is pointed out that there is nothing to prevent another season of heavy rain and hence that it is very essential that levelling up and drainage operations should be taken seriously in hand. Some of these present difficulties from the engineering standpoint and there is the usual scarcity of funds. As regards the use of larvicides petroleum has been found to have its limitations, for in pools exposed to high winds it gets blown aside leaving an

untreated water surface on which mosquitoes readily lay their eggs. Sanitas-okol answers admirably and recently izo-izal has been tried with a fair promise of success. Creosote does not seem to have any special virtue to commend it. Experiments have also been carried on with traps. Figures are given showing the type of these used in houses; they are based on the lines of those advocated for sandflies and consist of wooden boxes lined by a dark material or painted black inside. A hinged door closes the trap below and in this there is a hole, which can be closed by a metal slide, and through which fumigation can be conducted. These traps have so far proved useful and Balfour thinks would be certainly valuable, given any great prevalence of anophelines.

Stress is specially laid upon the danger of irrigated areas and on the part they play as attraction centres. When the Gezira to the south of Khartoum is irrigated on a large scale the Sudan Government will be face to face with a very serious problem, but the author believes that with due care and the wise expenditure of the necessary funds, together with the stringent enforcement of existing rules and regulations the problem can be solved.

The lesson which has been learnt in Khartoum is that in anti-malarial warfare the motto must be defiance not defence. It is necessary to go out to the attack, not to wait to be attacked.

[This is a very interesting and instructive paper and should be carefully studied by all those who are engaged in anti-malarial work both in damp and dry climates throughout the world.]

G. C. Low.

White (J. H.). **Malaria in Louisiana.**—*New Orleans Med. & Surg. Jl.* 1913. Aug. Vol. 66. No. 2. pp. 106-107.

The author proposes a scheme for concerted action between practitioners and the State Health Officer for the purpose of detecting and eventually wiping out malaria in Louisiana. He believes that many diseases, such as typhoid fever, &c., are at present erroneously classed as malaria owing to ignorance or slovenly diagnosis. He believes that if the measures he proposes are adopted complete success in the anti-malarial campaign will be obtained within a few years.

A. B.

Engeland (O.). **Meine Erfahrungen bezüglich der Malariaprophylaxe an Bord eines Kriegschiffes.** [My Experiences with reference to Malaria Prophylaxis on Board a War-ship.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. Aug. Vol. 17. No. 15. pp. 523-531.

This is an interesting account of a very thorough malaria prophylaxis carried out under the author's supervision on board a survey ship of the German Navy. The "Möwe" was for a period of 3½ months off the coast of South West Africa and called at many malaria-ridden ports. Engeland, as medical officer in charge of the ship, seized the opportunity of testing fully the

value both of mechanical protection and of quinine prophylaxis. He points out that what may be termed "personal" mechanical protection, *i.e.*, protection of the exposed parts of the body by veils, gloves, &c., is quite impracticable on board ship as it causes discomfort and interferes with work. It is impossible completely to protect a ship by mechanical means but these should supplement quinine prophylaxis. Before the latter came into general use the sickness and mortality returns from vessels of the German Navy employed on foreign service were very high. Latterly there has been a great change for the better, not only in the malaria rate but in the general sickness returns. Cases of blackwater fever and fatal cases of malaria are now very rare. There is still, however, evidence that quinine prophylaxis is not properly carried out. The author explains his procedure, which gave most gratifying results. He believes in employing both prophylactic measures. He began the systematic quinine prophylaxis seven days before reaching the first port where malaria was known to be prevalent and based his method of administration on Giemsa's statement that after 24 hours most, and after 72 hours all the quinine which has been taken is excreted. His object therefore was so to arrange matters that the men under his charge should always have quinine present in their circulating blood.

He employed the hydrochloride and in bad localities gave it every third day. When the ship was at sea or in harbours where malaria was not so rife the quinine was given every fourth day, the dose being one gramme. In his presence and under the direction of the officers of the watch nearly every man of the ship's crew took a tablet containing 0·5 grammes every second day at bedtime. The dose was washed down with acid solution to ensure its being absorbed. This was carried out from the middle of June to the middle of November, 1911. Men of the middle watch who were on duty between 12 p.m. and 4 a.m. took 0·5 grammes at night and the same dose next morning. There were a few exceptions, *i.e.*, in the case of stokers, &c., who had specially trying work.

Officers were treated by Nocht's fractional method [see paper by Justi in this number], taking the quinine at three or four days interval like the men. The prophylaxis was steadily continued after leaving the last harbour known to be malarious but the intervals were lengthened somewhat. The treatment terminated at the end of the eighth week. A certain number of cases proved unsuitable for the administration of quinine. These were men with poor digestions, bad teeth, neurasthenics and those who showed signs of quinine intolerance. Men coming under the first three headings were, as far as possible, prevented from going on shore expeditions, while intolerance was tested for by an initial dose of one gramme.

Sometimes, from quite unknown causes, quinine prophylaxis fails to avert malaria. Hence the necessity for mechanical protection which in any case is a useful adjunct. It was found that mosquitoes were frequently brought to the ship in water-supply boats, native crafts conveying vegetables, bum-boats, &c.

The following methods were carried into effect.

1. Whenever possible the ship anchored 1½ to 2 sea-miles from the land.
2. Leave of absence on shore was only granted during the day. Men were forbidden to enter native huts. Any members of the crew who had been ashore at night were each given one gramme of quinine on their return to the ship.
3. Fresh vegetables coming on board were immersed in water and the mosquitoes which they frequently harboured were thereby killed.
4. Covered native boats were not permitted alongside.
5. On the side where water and provision boats lay, all doors and windows were closed. After the departure of the boats the side was thoroughly washed down.
6. An energetic destruction of any mosquitoes which found access to the ship was carried out.
7. If the vessel had to be nearer than a sea-mile from land mechanical protection of port-holes &c. by means of gauze netting was employed. Wire gauze is not recommended. In the humid atmosphere of the West Coast it rusts rapidly, it is not easily repaired and it is much dearer than the ordinary netting. The latter should be fixed to frames of iron or wood and these should be covered by cloth to which the netting can easily be stitched. As Schilling states the mesh should not exceed 2 m.m. The netting should be in position by 6 p.m.
8. Only such lights as were absolutely necessary were permitted when the ship was near land.
9. The watch on deck wore mosquito boots and were allowed to smoke.
10. Survey parties on shore were provided with mosquito nets.

As a result of this careful system only one man of the ship's company (number, unfortunately not stated) contracted malaria. He was a cook and specially exposed to infection owing to the nature of his work, as the author explains. The prophylactic quinine failed in his case but the paper certainly shows what can be done by care and thoroughness.

A. B.

Giemsa (G.). **Das Mückensprayverfahren im Dienste der Bekämpfung der Malaria und anderer durch Stechmücken übertragbarer Krankheiten.** [The Mosquito-spray Method in the Campaign against Malaria and other Mosquito-borne Diseases.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. July. Vol. 17. No. 13. p. 456.

A note emphasizing the fact that the satisfactory experiments carried out at the Hamburg Institute as recorded by Giemsa in his previous paper [see this *Bulletin*, Vol. 2, p. 154] were obtained by the use of the pyrethrum preparation furnished by the Berlin firm of Riedel.* It is necessary to draw attention to this fact as adulterated preparations are inert. Mention is also made of a reduction in the price of the fluid, *i.e.*, from 2.65 to 2.38 marks per kilogram. A little further notice may be accorded Giemsa's former paper in which he describes the types of apparatus on the market.

These are made by the firm of Leonhard Schmidt, Grosser Burstah 46, Hamburg and there are three models, the first costing nine marks, the second and third 60 and 150 marks respectively. Model 1 is a hand-spray like a large garden syringe

* Address—J. D. Riedel A.-G., Berlin-Britz, Riedelstrasse.

and has interchangeable nozzles of varying form which can be fitted to the mouth piece so that different types of spray can be produced. Model 2 is in the form of a cylinder which can be carried on the back of the operator and holds ten litres of the special fluid. It works automatically under a pressure of five atmospheres. Model 3 is of a similar type but is larger, the container holding 30 litres and having a wheel and handles attached to it so that it can readily be moved about from place to place.

Giemsa points out that the efficacy of the method was shown by experiments on hibernating mosquitoes in cellars, stables, &c., in Hamburg and he recommends its use on a large scale for native huts which are so commonly infested by infected anophelines. Gangs of men armed with these sprays should systematically spray all native dwellings in malarial regions once every seven days, as it takes from eight to nine days for the malarial parasite to complete its cycle in the mosquito. It is important that the operators should work down-wind so that any mosquitoes which may have escaped destruction will not be blown back into huts already cleared but will more probably fly into those yet untreated and there meet their fate in due course. The method has an advantage over that of Ross in that, by its use, definitely infected imagines are frequently killed whereas anti-larval measures are directed against non-infected individuals and hence act in a more indirect manner. Its value in other mosquito-borne diseases (yellow fever, filariasis, &c.) is mentioned and it is stated to be beneficial in freeing plants from vermin as the fluid does not damage vegetation; the spray may perhaps find a use in destroying mosquitoes sheltering in plants and bushes in the neighbourhood of European dwellings.

[Giemsa's method is now employed on board Nile steamers at the quarantine station, Khartoum.]

A. B.

Experimental.

da Rocha-Lima (H.) & Werner (H.). **Ueber die Züchtung von Malariaparasiten nach der Methode von Bass.** [Cultivation of Malaria Parasites by the Method of Bass.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. Aug. Vol. 17. No. 16. pp. 541-551.

After mentioning the work of Nocht who, *in vitro*, was able to trace a partial development of malarial schizonts, *i.e.*, up to, but not beyond, the stage of sporulation, the authors record their own attempts and observations in 11 cases of tropical malaria and 6 of benign tertian fever. Like Bass they found the parasite of the former more easy to cultivate than the latter and they also agree that the best results are obtained when dextrose is added to the medium and the tubes are kept at room-temperature. They were, however, unable to substantiate *in toto* the results of Bass [this *Bulletin*, Vol. 1, pp. 22-24] or of those who support him, namely Ziemann and Thomson [this *Bulletin*, Vol. 1, p. 490 &

p. 648, and Vol. 2, p. 9 and pp. 224, 225]. This is evident from the following summary which gives the gist of their findings : —

1. They are unable to confirm Bass's complete work but can, like others, assert that his technique is useful for favouring a further development of a generation of malarial schizonts.

2. In the majority of 15 cases investigated they were able by Bass's method to trace this development up to the stage of division.

3. They failed to find evidence *in vitro* of any fresh commencing spore-forming cycles after the first division. They certainly saw in many cases, as long as 48 hours after the cultures were made, apparently vigorous, living, more developed forms of tertian and tropical [sub-tertian] schizonts, but these were traceable to a retardation of schizogony in the culture and did not proceed to a new second or third sporulation. They believe that Bass and the other observers mentioned drew faulty conclusions from what they saw and think that their own explanation is much more probably the correct one.

4. They could not observe a definite increase in the number of parasites. An increase is, however, easily simulated owing to the agglutination of infected red cells in the blood culture.

5. As noteworthy morphological peculiarities of the culture forms in tropical malaria they mention the fading of the erythrocytes which harbour the schizonts, a point already observed by Thomson, and the premature clumping of pigment in the schizonts which is usually complete before the division has commenced.

A. B.

Brown (Wade H.). **Malarial Pigment (Hematin) as an Active Factor in the Production of the Blood Picture of Malaria.**—*Jl. Experimental Med.* 1913. July 1. Vol. 18. No. 1. pp. 96-106.

The author refers to his previous experimental work* on hematin intoxication in the rabbit, which he showed to be characterised by the production of a paroxysm analogous to that of malaria. In this paper he considers the effect of the pigment not only on the formed elements of the blood but also upon the coagulation time and the bleeding time. Rabbits were again used and the solvent for the hematin consisted of a solution of 1 or 2 per cent. bicarbonate of soda in 0·85 per cent. sodium chloride solution. Control experiments were conducted to exclude any fallacy resulting from the action of the solvent itself. It was found that though the red blood corpuscles are less subject to the toxin action of hematin than either the leucocytes or the platelets they may yet be markedly reduced in numbers by its intravenous injection. The mechanism of destruction is not clear. *In vitro* haemolysis does not follow the addition of the alkaline hematin solution. This was to be expected in view of the hypertonicity of the solution. It frequently does occur in the animal body but does not depend entirely on the amount of hematin injected. The most marked effect is on the platelets, which are rapidly destroyed, and associated with this destruction there is often a tendency to persistent and even profuse haemorrhage. The other effects induced are sufficiently indicated by the author's summary from which it will be seen that he regards hematin as an active factor in the production of many, if not all, the important changes in the blood that characterise

* *Journal of Experimental Medicine.* 1912. Vol. 15. p. 579.

the various forms of malaria. In his opinion it is probably the hitherto unknown circulating toxin to which malarial anaemia has been attributed and he points out that the haemoglobin, converted to hematin by the malarial parasite, is not readily available for the regeneration of red cells and the blood is thus rapidly depleted of haemoglobin and iron, a condition tending to perpetuate the anaemic state. His summary is as follows:—

1. "Intravenous injections of alkaline hematin in the rabbit produce an anemia the severity of which is proportional to the amount of hematin injected and the susceptibility of the animal.
2. "Hemoglobinemia is an occasional consequence of hematin poisoning.
3. "The leucocytes in hematin intoxication are usually increased in number and are always characterized by a high percentage of large mononuclear cells and by pigmented phagocytes.
4. "The platelets are markedly reduced by alkaline hematin and ultimately a prolongation of the coagulation time of the blood and of the bleeding time results.
5. "The anemia, the hemoglobinemia, the high percentage of large mononuclear leucocytes, the destruction of platelets and the tendency to haemorrhage in malaria are all influenced by the malarial pigment hematin."

A. B.

Mosquitoes.

Strickland (C.). **Short Key to the Identification of the Anopheline Mosquitoes of Malaya for the Use of Medical Officers and others.** —15 pp. 1913. Kuala Lumpur, F.M.S. Government Printing Offices.

According to the author there are for all *practical* purposes 15 species of Malayan anophelines. Hitherto in the case of these, as of other mosquitoes, it has only been possible to determine the species by the use of elaborate synoptic tables. Strickland, however, has arranged a simple and ingenious key whereby the Malayan species may readily be determined by medical officers, sanitary board officers and planters even when an ordinary magnifying glass is alone available. It can only fail if a new species be discovered but he thinks its advantages outweigh this objection. In a few words the *exclusive* descriptions of each species are stated and rough drawings help the reader. Thus in one species attention is directed to the tufted abdomen, in several others certain characteristics of the hind-legs are alone sufficient for determination, in yet others the hind-legs and the proboscis are taken together. A group of four, including three *Myzorhynchus* and a *Neosthethopheles* can be distinguished from a study of their wings. The female palps form a guide to some, while, in others, the male palps plus the hind-legs furnish the clue. A note on the method of examination and a descriptive diagram of an anopheles, giving the male and female characteristics, serve as an introduction.

[While the key will doubtless fill a felt want, very few tropical sanitarians will agree with the opening paragraph of the author's preface which runs as follows:—"One can certainly eradicate malaria by wiping out all mosquitoes, for instance by a system of underground drainage a careful screening or destruction of all water holders, but why do this, when if one destroys these species

which cause malaria one gets the same result without having paid as well for the destruction of those which do no harm." It would have been better also if the illustrations of hind-legs on Plate VI had been drawn to a larger scale.]

A. B.

Mosquito Device.—*Canal Record.* 1913. June 11. Vol. 6. No. 42. p. 353.

An account of an ingenious contrivance for detecting the direction of the flight of mosquitoes. It is the invention of Mr. E. F. Quimby, an inspector in the Department of Sanitation, Canal Zone, Panama, and consists of a metal frame holding four plates of glass, each 12″ × 12″ in size, placed upon a tripod. These plates are held stationary at right angles to each other so that they are directed to the four points of the compass. To catch the mosquitoes they are smeared with a coat of tanglefoot made by adding half a pound of resin to a litre of castor oil. When smeared on the glass this coat is practically transparent. An all-night experiment with the apparatus showed "that the adult culex and anopheles flew on the quarter of a 17 to 19-mile wind; that the evening flight occurred between 6.10 and 7.10; that there was a complete lull in the flight after 7.10 o'clock; that there was a *return* flight between 5.50 and 6.40 in the morning, also on the wind's quarter; that the mosquitoes fly much higher and swifter in the morning than they do at night; and that, with possibly few exceptions, only adult females are in flight."

During another all-night test a single male anopheles was caught on the opposite side of the plates from the direction of the general flight. It is believed that it may have been flying about aimlessly when caught. "The instrument has proved to be useful in locating breeding places by eliminating the area facing the plates that do not show a catch. It also identifies the species of mosquitoes in the dark, as well as in the light, thereby determining the direction of flight, if any, during the night. Experiments show that there is no direct flight during the night, after a certain period. Further, this is the first time that a return flight has been recorded on the Isthmus; and it was shown to take place within a period."

An experiment tended to show that anopheles may fly low, slowly and in a zigzag flight as if seeking lulls in the wind.

A. B.

SLEEPING SICKNESS.

Macfie (J. W. Scott). **On the Morphology of the Trypanosome (*T. nigeriense*, n. sp.) from a Case of Sleeping Sickness from Eket, Southern Nigeria.**—*Ann. Trop. Med. & Parasit.* 1913. Aug. 11. Vol. 7. No. 3 A. pp. 339-356.

Sleeping Sickness was first discovered in the Eket district of Southern Nigeria early in 1912; by the end of April, 1913 a total of 167 cases had been identified. The disease does not seem to be of a virulent type in Nigeria and does not occur in epidemic form. To account for this fact it has been supposed that the disease must have existed for a great number of years and that the natives must have acquired a relative immunity.

Two phases of the disease are recognised: an early phase characterised by enlargement of the glands of the neck, and a later stage in which lethargy appears. Cases in the former stage are common, but those that have advanced to the latter stage are comparatively rare. The disease appears to be mild, although a number of deaths are reported to occur annually. The duration is a matter of years. The great majority of the patients are from 6-18 years of age; the sexes are about equally affected. As a rule the general health is good, there is no marked anaemia or wasting. Irregular fever occurs and is accompanied by the general symptoms of febrile disturbances. Skin rashes—urticaria and erythema—are present in many cases; but they are also common in uninfected natives. Impotence and amenorrhoea are said to accompany the disease. Enlargement of the cervical and axillary glands is a constant symptom. The natives believe that the disease is curable by excision of the glands, an operation which their 'doctors' readily perform. Numerous healthy individuals bearing scars on their necks are to be met with who have, it is affirmed, been cured in this manner. According to the natives the glandular phase of the disease lasts for about four years before lethargic symptoms develop. From the fact that somnolence is not a common symptom, most of the patients appearing to be in the early stages, it is possible that many of them recover before this stage is reached. Trypanosomes have been found in the gland juice of practically every case, but up to the present they have not been detected in the peripheral blood.

A brief description of the Eket district is given. The towns are generally some distance from the water. The children and young adults are the water carriers, this possibly accounting for the fact that they form the majority of the cases of sleeping sickness. Tsetse flies are prevalent all over the district; *G. palpalis*, *G. caliginea* and *G. tachinoides* have been found. Dr. Foran has observed that the tsetse flies 'appear to follow pigs about more than any other animal, and it is generally easier to catch the flies where these animals are than at the water.'

The strain of trypanosome.—A long and detailed account of the morphology of the trypanosome, as it appears in a guinea-pig, is given. There do not appear to be any features by which it can be distinguished from *T. gambiense* on microscopic examination. It is a polymorphic parasite, the individuals of which vary in

length from 8-34 microns; the average length is 21·5 microns. Posterior nuclear varieties have not been encountered. A biometric investigation of the trypanosome was undertaken, and 100 individuals of the infection in the guinea pig were measured on each of 10 consecutive days. In a chart the curve of the trypanosome is compared with that given by STEPHENS and FANTHAM for *T. gambiense*, and in a table the average, maximum, and minimum lengths and the percentage of short, intermediate, and long forms of the two parasites are compared. The author remarks that it will be observed that the trypanosome from Southern Nigeria is somewhat shorter than *T. gambiense*; the average length of 1,000 individuals being 21·5 microns as compared with 24·9.* The maximum and minimum lengths of this parasite are 34 and 8 microns as compared with 36 and 16 in the case of *T. gambiense*. The curve of this parasite is lower and more extended, and reaches its main peak at 21 instead of at 26 microns. The occurrence of extremely small individuals is characteristic of this strain.

Pathogenicity of the trypanosome.—Dr. FORAN at Eket inoculated a number of rats with the blood and gland juice of cases of sleeping sickness, but none of them became infected. Of six guinea-pigs only one had shown parasites in the peripheral blood to the time of writing; the infected animal was alive and well 124 days after inoculation. Of seven mice three showed trypanosomes in the peripheral blood after incubation periods of 4, 6 and 8 days, respectively; parasites had not been seen in the others up to the time of writing. Two goats were negative up to the 24th day, as were also two dogs. A monkey became infected on the 10th day and was alive and well on the 22nd day after inoculation.

In conclusion the author considers that this trypanosome differs in several respects from *T. gambiense*. In man it produces a form of sleeping sickness that is relatively mild, and occurs most commonly in young people. Trypanosomes are apparently either absent from the peripheral blood altogether, or present in such small numbers that hitherto they have not been detected. To the smaller laboratory animals the strain is but slightly pathogenic. The trypanosome is smaller than *T. gambiense* and there appear constantly in the blood films a few very minute parasites measuring as little as 8 microns in length. It is stated that the occurrence of a few peculiar trypanosomes which appear to have a flagellum free in their whole length is remarkable.

The author is convinced that this trypanosome from Nigeria cannot be regarded as belonging to the same species as *T. gambiense* and proposes for it the name *T. nigeriense*.

[The most important part of this paper is that dealing with the recognition of a chronic form of trypanosomiasis in children and young adults. The author has come to the conclusion that the chronicity is to be explained on the ground that the pathogenic agent is a new human trypanosome. The evidence he advances to support this view is, however, inconclusive. The parasite was

* STEPHENS and FANTHAM'S measurements were from rats.

examined in one guinea-pig only and the points of differentiation mentioned by the author would hardly justify a description of a new human trypanosome. The anterior displacement of the nucleus is seen in other trypanosomes and the flagellum 'free in its whole length' is also frequently to be observed in many species of trypanosomes and is probably an artefact. The chronicity of the disease might equally well be explained by the assumption of a special tolerance on the part of the host.]

W. Yorke.

Hearsey (H.). **Nyasaland Sleeping Sickness Diary.** 1913. April 30. Part 20. 11 pp. Zomba: Government Printers.

An account is given of 20 additional cases of human trypanosomiasis reported during the period January to April, 1913. Nineteen of these were found in the sleeping sickness area and one near Kotakota in the Marimba district. Fourteen of the 20 patients have died, as have also cases 105 and 106. To the time of writing 128 cases of sleeping sickness had been discovered in Nyasaland. Clearing of bush and scrub is being carried out around all villages in the sleeping sickness area. A re-investigation of the districts to the north and south of the Proclaimed area is shortly to be undertaken in order to ascertain whether these localities harbour cases of sleeping sickness.

W. Y.

Eckard (B.). **Ueber Schlafkrankheit.** [On Sleeping Sickness.] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1913. July. Vol. 17. No. 14. pp. 494-497.

The author states that the view is generally held that the onset of sleeping sickness is so extremely insidious that a person may be infected for months or years without the cognizance of either himself or the doctor. He quotes Mense's handbook on tropical diseases in support of this statement.

As the result of his personal experience in German East Africa the author is convinced that sleeping sickness commences acutely with the most violent symptoms (*stürmischsten Erscheinungen*) about 14 days after the infective bite. Various cases (5 native, 2 European and 1 Indian) in which the approximate date of the infective bite could be determined are quoted in support of this contention. High temperatures and rigors were prominent symptoms. The results of treatment of these eight cases are peculiar. Whilst in the natives the trypanosomes disappeared after the first injection of atoxyl and the patients after one or two atoxyl treatments remained cured, the infections in the Indian and the two Europeans proved from the commencement to be atoxyl fast. Whether the strain was more virulent in the latter or whether these are more susceptible than the natives the author is unable to state. It might be mentioned that in Rhodesia and in the southern district of German East Africa the human infections appear to be rather atoxyl fast. The author goes on to describe the course of the disease.

W. Y.

Ungulates and Sleeping Sickness.

Kleine (F. K.) & Eckard (B.). **Ueber die Bedeutung der Haustiere und des Wildes für die Verbreitung der Schlafkrankheit.** [On the Significance of Domestic Stock and Game for the Spread of Sleeping Sickness.]—*Zeitschr. f. Hygiene u. Infektionskr.* 1913. July 17. Vol. 75. No. 1. pp. 118-122.

These investigations are a continuation of the work of Kleine and Fischer (*Sleeping Sickness Bulletin*, Vol. 3, p. 402). Of 13 experiments, in which infective *G. palpalis* were fed on healthy goats and sheep, 9 were negative, whereas in control experiments in which monkeys were used all became infected. These experiments indicate the difference of susceptibility of monkeys and domestic stock. [These results should be compared with those of Duke (see this *Bulletin*, Vol. 2, p. 240).] Goats and sheep would appear to have but little significance as a reservoir of the infection. *G. palpalis* could not be infected on three of seven animals in which *T. gambiense* was found in the blood. The infectivity diminished with the length of time which had elapsed from the first appearance of trypanosomes in the blood.

The authors had the opportunity of examining two of these goats, 73 and 89, again. They were infected in September, 1910 and in March, 1912 no parasites were found in the blood. Several blood injections into monkeys were negative. From April 9 to August 3, 1912, a large number (744) of laboratory bred *G. palpalis* were fed on Goat 73 and subsequently on healthy goats. All the flies were examined, but no trypanosomes were found. The goats were hence cured. Goat 73 was reinoculated from a sleeping sickness monkey, but did not become infected; after a second reinoculation a single trypanosome was once found in its blood. Goat 89 became ill after the first reinoculation and again after the fourth, but subsequently recovered. Resistance and immunity against *T. gambiense* were further demonstrated. A number of goats, sheep and cattle were repeatedly inoculated with virulent blood. Only 10 of 21 animals became ill after the first injection, 5 after the second, 4 after the third, 1 after the fourth and 1 remained healthy. Parasites were only rarely found in the blood of infected goats and in small numbers. Often the incubation was very long—in one sheep over 46 days. The experimental animals always remained in good condition and exhibited no signs of disease.

The authors examined 113 mammals from sleeping sickness districts on Tanganyika; 15 cc. of blood from the jugular vein or heart were injected into healthy monkeys. Twenty-three bushbuck, one hippo, and four bushpig were found to be negative. Trypanosomes (*T. cazalboui* or *T. nanum*) were found in the blood of two bushbuck. Five cattle, 55 goats and 25 sheep were examined from districts heavily infected with sleeping sickness and of these 1 ox, 1 goat and 1 sheep (*i.e.*, 3·5 per cent. of the domestic stock or 2·5 per cent. of the total mammals examined) were found to be infected with *T. gambiense*. Parasites of the *cazalboui* type were found in 3 oxen, 2 goats and 1 sheep.

As a result of these investigations the authors are of opinion that domestic animals play a much less important part as reservoirs of sleeping sickness than human beings. Although the authors did not find *T. gambiense* in game, yet Duke has shown that natural infections do occur in antelopes. General measures are, however, unnecessary on account of the relatively small percentage infected, especially in those districts where the disease is mainly spread by *G. palpalis*. Whether and where the game should be destroyed must depend on local conditions. The chief significance of the game as parasite carriers lies, in the authors' opinion, in the fact discovered by Bruce that in regions from which the human inhabitants have been completely removed on account of sleeping sickness the infection has not died out after several years.

With regard to *T. rhodesiense* the circumstances are not so clear, as this parasite is at present indistinguishable from the cattle trypanosome *T. brucei*. The view of Kinghorn and Yorke that in the Luangwa Valley of Northern Rhodesia 16 per cent. of the game is infected with *T. rhodesiense* is extremely improbable, as they failed to find the morphologically similar and widely spread *T. brucei* in such a definite *morsitans* country.

The authors have considered the question as to whether *T. brucei* may not exceptionally become virulent for men and whether the insusceptibility of adults may not be due to slight infection during childhood. They have so far found no support for this supposition; about 500 children were examined in *morsitans* districts without finding any case of trypanosomiasis. [The authors are evidently unaware of the opinions expressed by the Royal Society Commission to Nyasaland and others that *T. rhodesiense* is identical with *T. brucei* or *T. ugandae* (Stephens and Blacklock).]

W. Y.

Taute (M.). **Untersuchungen über die Bedeutung des Grosswildes und der Haustiere für die Verbreitung der Schlafkrankheit.** [Investigations on the Significance of Big Game and Domestic Stock for the Spread of Sleeping Sickness.]—*Arbeit. a.d. Kais. Gesundheitsamt.* 1913. Aug. Vol. 45. No. 1. pp. 102-112. With 1 plate.

In view of the great divergence of opinion as to the practical significance of big game and domestic stock in the campaign against sleeping sickness these investigations were undertaken especially with a view to examining the work of Kinghorn and Yorke, who found that in the Luangwa Valley of Northern Rhodesia 16 per cent. of the game were infected with *T. rhodesiense*.

The experiments were carried out at Lubimbinu in Portuguese Nyasaland about 90 km. from Fort Johnston and about 600 m. above sea-level. Lubimbinu is itself fly-free, but is surrounded by a large wooded fly belt in which *Glossina morsitans* was present in enormous numbers and in the rainy season Tabanids were plentiful. The population is free from trypanosomiasis, but quite

the reverse is the case with domestic stock. Cattle and sheep are not found, goats are rare, and dogs are very seldom seen and rapidly die.

The experimental animals were brought from fly-free areas in fly-proof boxes and only used after a sufficient period of quarantine; monkeys and dogs were chiefly used.

Rhodesiense-like trypanosome in big game.—From the end of August until the end of December, 1912, 37 wild animals, including buffalo (1), eland (1), zebra (2), waterbuck (10), hartebeest (12), bushbuck (3), reedbuck (2), duiker (4), warthog (1) and bushpig (1), were examined in the above district. The results of direct examination of the blood and of the subinoculations into monkeys, dogs and goats are given in a table. Trypanosomes were found by direct examination in 19 instances. Of the 25 subinoculations made into monkeys and dogs 6 were positive and of the 3 made into goats 1 was positive. Of the 37 animals examined trypanosomes were found either by direct examination or by subinoculation or by both methods in 20. Trypanosomes similar morphologically, and as regards their pathogenicity, to *T. rhodesiense* were found in 6 of the subinoculated monkeys and dogs. The rest of the trypanosomes found in the game belonged to the groups *T. vivax* and *T. pecorum*.

Rhodesiense-like trypanosomes in domestic stock.—In 369 wild *Glossina morsitans* examined mammalian blood was found in 69 (18·7 per cent.) and developmental forms of mammalian trypanosomes in 27 (7·3 per cent.). In 10 experiments 1,069 wild *Glossina morsitans* were fed in batches on 8 dogs and 2 monkeys and 6 of the animals became infected with a polymorphic trypanosome exhibiting posterior nuclear forms in 4-6 days. Seven dogs and one goat were purchased in the villages situated in the fly belt and all were found to be infected with a polymorphic trypanosome exhibiting posterior nuclear forms. Two other goats were found to be infected with a trypanosome non-pathogenic for monkeys and dogs which was probably *T. vivax*.

The author gives a detailed description of the trypanosome found in the antelope and domestic animals. It is a polymorphic parasite exhibiting posterior nuclear forms and indistinguishable morphologically from *T. rhodesiense*. The maximum, minimum and average lengths of 2,000 individuals were 36, 13 and 21·8 microns, respectively. These figures are compared in a table with those obtained by Bruce, Stephens and Fantham, and Kinghorn and Yorke for *T. rhodesiense* from men and with those obtained by Kinghorn and Yorke for the antelope strain of *T. rhodesiense*. The biometric curve obtained by the author is also compared with those of Kinghorn and Yorke, and Bruce and his colleagues.

The pathogenicity of the trypanosome was examined and the average duration of the disease was in 36 dogs 17 days, in 12 monkeys 23 days, in 9 goats 16 days and in 5 rats 24 days. Three oxen were still alive on the 29th day, but all showed signs of disease. Infected dogs and goats showed interstitial keratitis and a characteristic oedema of the face.

Experimental separation of the antelope and domestic stock trypanosome from true T. rhodesiense.—The author remarks that if the view of KINGHORN and YORKE be correct that the trypanosome in question is really *T. rhodesiense*, then in this locality 16·2 per cent. of the game and an almost equal proportion of domestic stock were infected with it in spite of the fact that no case of human trypanosomiasis has been discovered in the district. Thus the game would here not only act as a reservoir, but also as a precursor of Sleeping Sickness. To prove that this view is erroneous the author performed the following experiment on himself. Ninety-three laboratory-bred *Glossina morsitans* were fed for 4 days on a monkey infected with the antelope strain and after starving for a day were fed on a series of healthy animals, as in the table.

TABLE III.

No. of flies.	Flies fed		Result.	Course of disease.	Remarks.
	From	On			
74	6th–12th day	Goat No. 16...	Goat remained well.	—	—
61	13th–16th „	Goat No. 22...	„ „	—	—
52	17th–19th „	Goat No. 34...	„ „	—	—
45	20th–22nd „	Goat No. 43...	Goat developed trypanosomiasis.	Died on 20th day of infection	Well-marked posterior nuclear forms found in blood.
39	23rd–25th „	Monkey No. 75	Monkey developed trypanosomiasis.	Died on 25th day of infection	
34	26th–27th „	Dog No. 51 and Dog No. 76.	Both dogs developed trypanosomiasis.	Dog No. 51 became blind on the 16th day and died on 19th day of infection. Dog 76 showed keratitis on 14th and died on 24th day of infection.	
32	28th–32nd „	Man [TAUTE]	Man remained well.	—	—
31	33rd–35th „	Monkey No. 72	Monkey developed trypanosomiasis.	Died on 14th day of infection.	Well-marked posterior nuclear forms found in blood.
29	36th–40th „	Dog No. 71...	Dog developed trypanosomiasis.	Died on 8th day of infection.	
27	41st–44th „	Dog No. 33...	Dog developed trypanosomiasis.	Showed keratitis on 13th day and died on 21st day of infection.	

In a second and similar experiment 77 laboratory-bred flies were allowed to feed for 4 days on 5 animals infected with 5 different antelope strains; the subsequent procedure was similar to that described above. The author did not become infected.

In a further experiment 2 cc. of the blood from a naturally infected dog was injected into the author and also in various amounts (2 cc. or less) into a monkey, 3 dogs, a goat and 2 rats. The author remained healthy whilst the experimental animals all became infected and died.

These experiments show that a trypanosome, from wild game and domestic stock, indistinguishable from *T. rhodesiense* does

not infect man either when infected flies are allowed to feed upon him or by direct inoculation of the infective blood. Reference is made to the work of Wenyon and Blacklock who showed that posterior nuclear trypanosomes were to be found in *T. pecaudi* and *T. brucei*. The author considers that the game and domestic stock trypanosome is *T. brucei*. He refers to the somewhat similar experiment recorded by Todd (*Sleeping Sickness Bulletin*, Vol. 3, p. 174)* in support of this opinion. In order to demonstrate that he was not infected the author inoculated 90 cc. of his blood in doses of 2-15 cc. into a monkey and 7 dogs; these did not become infected. The paper concludes with the remark that *T. brucei* cannot live in the human body.

The conclusions are:—

Trypanosomes in naturally infected game and domestic stock can only be regarded with certainty as the cause of Sleeping Sickness when they have been shown to be pathogenic for man.

The game and domestic animals do not at least play the part in the spread of sleeping sickness supposed by Kinghorn and Yorke.

In judging of the infectivity of a region with Sleeping Sickness it is not sufficient merely to prove that the bite of the wild *Glossina* gives rise to an infection in experimental animals with an apparently identical trypanosome.

In the east Nyasaland area *T. brucei* can be distinguished from the pathogenic agent of Sleeping Sickness only by the fact that it is non-pathogenic for man; it rapidly dies in the human body.

[These experiments are obviously of great value, but it is doubtful if they establish the point which the author wishes to prove, namely, that the antelope trypanosome is different from the human parasite, *T. rhodesiense*. All the author has proved is that a healthy human individual has been able to resist infection. A possible interpretation of the facts is that at the present time the normal human being is able to offer considerable resistance to infection with *T. rhodesiense* and hence it is only occasionally that a case of infection occurs.]

W. Y.

Treatment.

Kolle (W.), Hartoch (O.), Rothermundt (M.), & Schürmann (W.). **Chemotherapeutische Experimentalstudien bei Trypanosomen Infektion.** [Chemotherapeutic Experimental Studies in Trypanosomiasis.]—*Zeitsch. f. Immunitätsforsch. u. experiment. Therapie.* 1913. Aug. 5. Vol. 19. No. 1. pp. 66-97.

Most of the work recorded in this paper has been published previously (see this *Bulletin*, Vol. 2, pp. 134 and 249). In these papers, which dealt with various preparations of antimony as therapeutic agents in trypanosomiasis, it was pointed out that "Trixidin" (antimony trioxide) was of remarkable value. It

* This experiment, in which blood from a trypanosome infected cow was injected into a European and two natives without untoward effect, differed in that there is nothing to show what the species of trypanosome was. It might have belonged to the *vivax* or *pecorum* group.—A. G. B.

was practically non-poisonous in the doses used and of great therapeutic efficacy. In a table is shown the effects of large doses of trixidin on normal mice. It was found that 240 mgm. of the drug killed mice of 15 and 17 gm. on the 2nd and 3rd day, respectively, but a dose of 120 mgm. per 10 gm. of body weight was well borne by the animal and no symptoms of acute or chronic poisoning resulted. In another table is given the result of treating 12 mice, infected with nagana, with trixidin. In this series of experiments it is shown that 1 mgm. of the drug is sufficient to cure the mice and prevent relapses.

Experiments were also carried out to ascertain whether trixidin had any prophylactic action against infection with trypanosomes. The results of these experiments are shown in tables. The drug prevented infection in a great proportion of cases and in certain animals infection did not occur when they were inoculated with a virulent strain of nagana sixteen days after the drug had been administered.

The second portion of the paper deals with the cutaneous administration of insoluble antimony compounds in ointment form. The results of treating infected mice by systematic daily inunctions of 50 per cent. metallic antimony ointment, or with 40 per cent. dimethylphenylpyrazolonacethylantimony ointment are given in tables. By this method the authors succeeded in curing between 60 and 70 per cent. of mice infected with nagana, dourine, or *T. gambiense*.

In a postscript the authors write that they carried out experiments on animals infected with the spirochaete of African relapsing fever. These preparations of antimony whether administered intramuscularly or by inunction had no effect on this parasite. Similar negative results were obtained in the case of mice infected with *Schizotrypanum cruzi*.

In their conclusions the authors state:—

The toxicological actions of antimony compounds—soluble and insoluble—require further study, especially in regard to organotropy and chronic poisonous effects.

Antimony compounds are chemotherapeutically active only when they contain the antimony in the trivalent form. Antimony trioxide, "Trixidin," is of all hitherto known antimony preparations the most active in intramuscular injection. By one or two intramuscular injections of absolutely nonpoisonous doses of "Trixidin" 100 per cent. of mice infected with nagana can be permanently cured.

Metallic antimony also cures infected mice, but gives rise to chronic poisoning ending in death. Administered, however, in ointment form it is equally efficacious and is not poisonous.

The organic insoluble compound "Dimethylphenylpyrazolenantimony-chloride" is also, when administered in ointment form, a remedy which permanently cures without the slightest poisonous effects.

The formation of depots of insoluble, slowly absorbable compounds of antimony such as antimony trioxide acts prophylactically against infection with trypanosomes.

As a result of these experiments the treatment of chronic trypanosome infections by repeated administrations of insoluble, slowly absorbable, antimony preparations in combination with other remedies is recommended, in order to obtain through slow but continuous absorption a lasting action and permanent cure.

W. Y.

Tanon (L.) & Dupont (A.). **Traitement de la Trypanosomiase humaine.**—*Bulls. et Méms. Soc. Méd. des Hôpit. de Paris.* 1913. May 15. 3 ser. Vol. 29. No. 16. pp. 975-988.

An account is here given of the therapeutic action of two new derivatives of arsenic—1116 (tétraoxydiphosphaminodiarsénobenzène) and 1151 (phényldisulfaminotétraoxydiaminodiarsénobenzène)—in trypanosome and spirochaete infections in experimental animals and man.

Experiments were carried out with rats, mice, guinea-pigs and *Macacus rhesus* infected with *T. gambiense*, and rats and mice infected with *Sp. duttoni*. The animals infected with *T. gambiense* were cured in two or three hours after a subcutaneous injection of 1116 or 1151. The drugs were given in the following doses:—mice ·001 gm. per 10 gm. of body weight, rats ·02 gm. per 100 gm. of body weight and monkeys ·1 gm. per kilo of body weight. The injections provoked some slight local reaction which disappeared in 3 or 4 days. For subcutaneous administration the salt was dissolved in distilled water in the proportion of ·05 gm. per 10 cc. In these doses the drugs caused the trypanosomes to disappear rapidly and no relapse was noted in any of the 500 animals used by the authors.

An account is given of the manner in which the parasites are destroyed. The phenomena were studied *in vivo* and *in vitro*: the disappearance of the trypanosomes is due to trypanolysis and not to phagocytosis. In the case of spirochaetes fragmentation precedes spirillolysis.

The value of the drugs was tested on sleeping sickness patients in Senegal. In all, 30 cases were treated and the authors are able to record 15 as definitely cured. Those probably cured are more numerous, but the lack of experimental animals has obliged the authors to delay publication regarding several of these. Only those cases were treated in which trypanosomes had been definitely found in the blood or glands. Four injections of 1151 or 1116 dissolved in 3 cc. of 12 or 15 per cent. sodium carbonate serum were given at intervals of 8 days; 25 per cent. carbonate serum was also employed, but such solutions caused vomiting. The drug was given intravenously, as subcutaneous or intramuscular injection caused considerable pain. Administration per os was found to be valueless. A month later the blood and gland juice were examined and if no trypanosomes were found 10 cc. of blood and 10 cc. of cerebro-spinal fluid were injected intraperitoneally into a monkey (*Cercopithecus ruber* or *patas*). If the monkey proved not to be infected at the end of 40 days the patient was considered to be cured. Details are given of six cases cured, the authors say, by means of 1116 or 1151. Treatment is easy and the drugs are well borne by the patients, nor do there appear to be any serious accidents following the injections. The vomiting and diarrhoea, sometimes noticed, may be attributed either to the drug itself or, as the authors are inclined to think, to the hyperalkalinity of the serum employed. These symptoms were more noticeable after administration of the 25 per cent. carbonate serum than after the 12 or 15 per cent.

These drugs were found to cure the disease in the 1st and 2nd stage, but not in the 3rd stage when the cerebro-spinal system is involved, as they penetrate but slowly into the cerebro-spinal fluid. Possibly injections of the diluted drug into the cerebro-spinal canal might prove successful, but experiments are necessary.

W. Y.

Laveran (A.) & Roudsky (D.). **Le Galyl dans les Trypanosomiases.**—*Bull. Soc. Path. Exot.* 1913. July. Vol. 6. No. 7. pp. 502-505.

The authors refer to the work of Tanon and Dupont (see above) which showed that two new arsenical compounds 1116, or galyl, and 1151, or ludyl, were of considerable therapeutic value in animals and man infected with *T. gambiense.* In the present paper the action of galyl was tested on animals infected with other pathogenic trypanosomes. Galyl is a yellow powder which is insoluble in water, but a solution is readily obtained if sodium carbonate is added to a fine suspension of the drug in distilled water. Solutions of the following strengths were injected intramuscularly—in mice and rats 1 in 200 and in guinea-pigs 1 in 100. There is only slight local reaction in the former animals, but in guinea-pigs the reaction is more marked, painful on pressure and lasts for several days. In mice of 20 gm. up to 1·5 mgm. can be given; in healthy mice 2 mgm. can frequently be given, but infected mice are more sensitive and 1·5 mgm. sometimes kills. This is probably due to the combined poisonous effects of the drug and toxins liberated from the disintegrated trypanosomes. In guinea-pigs 1 cgm. can be given for each 100 gm. of body weight. The drug was tested on animals infected with the following trypanosomes:—*T. brucei* (nagana ferox, Ehrlich), *T. evansi, T. rhodesiense, T. gambiense, T. soudanense, T. hippicum, T. dimorphon, T. congolense,* and *T. pecorum.* Galyl was found to be very active in infections of *T. brucei, T. evansi, T. rhodesiense, T. soudanense, T. gambiense* and *T. hippicum.* It was, however, quite inactive in the case of *T. dimorphon, T. congolense* and *T. pecorum.* Ludyl was equally inefficacious in the case of *T. dimorphon.*

The authors point out that the activity of a drug is often more marked on one species of trypanosome than on another, but it is exceptional to find such a clearly cut distinction between sensitive and refractory trypanosomes as occurs in the case of this drug. The fact that galyl is inactive for *T. dimorphon, T. congolense* and *T. pecorum* shows once more that these parasites are closely related.

W. Y.

Ritz (H.). **Chemotherapeutische Versuche mit "Trypasafrol."** (Zum Teil nach Versuchen von Frl. F. Leupold.) [Chemotherapeutic Experiments with Trypasafrol.]—*Berlin Klin. Wochenschr.* 1913. July 28. Vol. 50. No. 30. pp. 1387-1389.

The author refers to the work of Brieger and Krause (see *Sleeping Sickness Bulletin* Vol. 4. p. 328) on treatment of experimental trypanosomiasis with a dye of the safranin series

called by them 'Trypasafrol.' The results of these workers appeared so satisfactory that Ritz decided to repeat the experiments. The technique employed was that of Brieger and Krause. Infected animals were fed on food with which trypasafrol was mixed. In a further series of experiments, in order that the exact dose administered might be known, a solution of the dye was passed into the animals' stomach by means of a tube. Two strains of *T. brucei* were used, (1) Morgenroth's which is extremely sensitive to arsenic and exhibits a normal sensitiveness to dyes, (2) the Ferox strain of Ehrlich which is partially arsenic-fast.

The lethal dose of the dye was first ascertained. It was found that when the drug was administered by means of the stomach tube 0·5 gm. per kilo of body weight was fatal for guinea-pigs and 0·4 gm. was not always well borne. The lethal dose in mice was approximately 0·01 gm. per 20 gm. of body weight. About 0·06 gm. was found to be toxic when administered more gradually, mixed with the food.

The results of the experiments on mice, rats and guinea-pigs are given in four tables. Only a single mouse was cured. The author writes that trypasafrol does not cure mice, rats and guinea-pigs experimentally infected with the strains of *T. brucei* used by him. It appeared to exert a slight effect in mice, as the course of the disease was somewhat prolonged and one mouse out of 19 was cured. It was observed that 60-70 per cent. of trypanosomes in the treated animals lost their blepharoplast.

W. Y.

Immunisation.

(i.) Rondoni (Pietro) & Goretti (Guido). **Studien über Schutzimpfung gegen experimentelle Naganainfektion.** [Studies on Vaccination against Experimental Nagana Infection.]—*Zeit. f. Immunitätsforsch. u. experim. Therapie.* 1. Teil. Orig. 1913. July 17. Vol. 18. No. 5. pp. 491-515.

(ii.) **Ricerche Sperimentali sul Nagana.**—*Lo Sperimentale.* 1913. Aug. 16. Vol. 67. No. 4. pp. 427-453.

These papers are identical and give an account of attempts to produce active immunity in respect to infections by *T. brucei*. The authors express their conviction that in order to obtain successful immunity one should attempt to damage as little as possible the substance of the body of the trypanosome, to which the antigen property is bound. The trypanosomes must be killed or rendered innocuous in such a manner as to preserve the integrity of their receptors.

The authors adopted four procedures: treatment of the trypanosome suspension with (1) distilled water, (2) hypertonic solution of NaCl, (3) salts of quinine, and (4) salvarsan. White mice were used chiefly for the experiments. A virulent strain of nagana was employed and the trypanosome suspension obtained from rats by fractional centrifugation of their blood when heavily infected.

The administration of vaccines prepared by use of methods (1), (2) and (3) caused a definite prolongation of the incubation

period on subsequent (3-8 days later) injection of virulent trypanosomes and death occurred several days later than in the case of the controls. But by each method no absolute immunity was produced.

Vaccines prepared with salvarsan (Method 4) gave good results. The authors found that between the strengths of salvarsan which killed the trypanosomes outright, and that which merely weakens them without rendering them innocuous, there was an intermediate strength which although it did not cause their death, yet was sufficient to render them quite incapable of multiplying in the animal body. The experiments described show that there must be a definite quantitative relationship between the salvarsan and trypanosomes employed in order to obtain a successful vaccine. The salvarsan must be fresh and cannot be used after 10 or 15 days. Two large white rats were bled at the height of the infection, and the blood collected in citrate of sodium broth and centrifuged gently. The liquid containing the majority of the trypanosomes and a few red cells was mixed with a solution of salvarsan in such a manner as to make a dilution of salvarsan 1 : 40,000. The emulsion was kept half an hour at room temperature to permit the combination of the arsenical product with the trypanosomes. After this period the latter appear well preserved and mobile. It is advisable to choose such a dose of salvarsan as causes a slight slowing of movement, in order to be practically certain of the avirulence of the parasites and avoid accidental infection and loss of the animals. After strong centrifugation the sediment is taken up in a little salt solution. This constitutes the vaccine and is injected intraperitoneally into mice. If mice treated with this salvarsan-vaccine are later inoculated, many remain free from parasites (observation several weeks), others show parasites and die a long period after the controls. Forty to fifty per cent. of animals vaccinated a single time with this salvarsan-vaccine are completely refractory to subsequent inoculations with small doses of trypanosomes. A table containing the results of the experiment is given; 18 mice including 3 controls were used. The serum of rabbits treated with the vaccine possesses marked trypanocidal properties. The authors consider it desirable to extend these researches and apply them to other species of trypanosome, as such a method might give practical results of some importance.

W. Y.

Schilling (Claus) & Rondoni (Pietro). **Ueber Trypanosomen-Toxine und-Immunität.** [On Trypanosome Toxin and Immunity].—*Zeitschr. f. Immunitätsforsch. u. experim. Therapie.* 1913. July 26. Vol. 18. No. 6. pp. 651-665.

Reference is made to the observation of Schilling that a suspension of nagana trypanosomes which had been allowed to stand for some hours at 37° C. is exceedingly toxic for mice and rapidly causes death. A heavily infected nagana rat was bled into 2 per cent. sodium citrate bouillon (1 part blood to 4 parts citrate bouillon); the suspension was kept at 37° C. in a water bath. The

trypanosomes, which were at first actively motile, had at the end of 3 hours become almost completely immobile. The microscopic appearances of the degenerated trypanosomes are described. Mice were inoculated intraperitoneally with ·25 cc. of the suspension after it had been kept at 37° C. for the following periods, viz., ½ hr., 1 hr., 3 hrs., 5 hrs. and 7 hrs. Those inoculated with the suspension which had been kept up to 3 hours became infected and died from the infection, whereas those inoculated after 5 and 7 hours respectively did not become infected, but nevertheless died. All those inoculated after 7 hours died the following night. A second series of experiments was performed in which the trypanosomes were separated from the bouillon and blood by centrifuging and then added to fresh bouillon. In this case the trypanosomes were found to die more quickly, so that at the end of one hour there was at the most only a trace of movement. Apparently the centrifugation had to a certain extent damaged the trypanosomes; the suspension was not infective after 1¼ hours. However, so much toxin had been formed after 2¼ hours that one of 2 mice died in 48 hours; after 4¼ hours it killed mice within 24 hours. Experiments were undertaken to show that the poison came from the trypanosomes only and not from the blood or medium. The poison was found to develop equally well when the suspension was kept at 45° C. for 4 hours, but did not develop at 56° C. Further experiments demonstrated that bacterial contamination was not responsible for the toxin formation.

The lethal dose is dependent on two factors: first the number of trypanosomes in the suspension and secondly the individual variations in the experimental animals.

The poisonous suspension was centrifuged and the deposit of disintegrated trypanosomes and the clear supernatant fluid containing the soluble constitutents of the parasites were injected into different series of mice. Only those died into which the deposit was injected. When the suspension was allowed to stand at 37° C. for more than 8 hours the toxic effect began to disappear and after 18 hours it was almost completely lost. The poison is thermolabile, losing its toxicity in ½ hour at 56° C.; on the other hand it remains active many days when kept in the ice chest. Its action is destroyed by the addition of carbolic acid.

The poison from the trypanosomes acts as antigen. A proportion of mice treated with a non-lethal dose remained alive when subsequently, after 5-6 days, inoculated with a lethal dose sufficient to kill the control animals in 1-2 days. Doses of ·0005-·001 cc. suffice to raise the resistance of the animals considerably. Further experiments were undertaken to ascertain whether the poison which had been inactivated by heating to 56° C. or by the addition of carbolic acid was still capable of acting as antigen. This proved to be the case and hence it was shown that the toxic function and the antigen function of the warmed trypanosome suspension are different.

It is of interest to observe that such antibodies are formed very early in the course of nagana infection in mice. This point is illustrated by experiments in which it was shown that mice which

were injected with infective blood + toxin did not die from the poison, but only later from the infection.

The authors were unable to demonstrate poisonous effects of suspensions from non-pathogenic trypanosomes such as *T. lewisi.* Definite results were not obtained with *T. equiperdum,* but these experiments are to be repeated. In the case of *Sp. duttoni* the authors were able to demonstrate the formation of a toxin in suspensions which had stood for 4 hours at 37° C., but doses of ·25 cc. did not always kill mice within 18 hours.

It has been shown by the experiments of Teichmann and Braun (*Sleeping Sickness Bulletin,* Vol. 4, p. 58), and also by those of Schilling that the bodies of trypanosomes contain immuno-antigen which when introduced into a susceptible animal gives rise to a more or less marked degree of immunity against living trypanosomes. Six mice which had been treated with ·25 cc. of trypanosome suspension (warmed at 37° C. for $1\frac{1}{4}$-$1\frac{3}{4}$ hours) were inoculated 7 days later with infective blood. The animals did not become infected. This experiment shows that immuno-antigen is present before a demonstrable amount of toxin is formed in the warmed trypanosome suspension. Another series of mice was treated with non-lethal doses (·04–·1 cc.) of the poisonous suspension and 7 days later inoculated with infective blood. Of the 9 animals thus treated 6 remained free from infection. Still better results were obtained by injecting in the first place a non-lethal dose of the poison or one which had been inactivated by heating to 56° C. and subsequently repeating the injection with a larger amount of the poison.

When the poisonous suspension was passed through a Berkefeld filter the filtrate was no longer toxic, but nevertheless served as immuno-antigen. The immuno-antigen is not destroyed by heating to 37° C. for 18 hours, whilst as already mentioned the toxin is destroyed. It was found that the carbolised poison protected against the subsequent injection of the toxin but not against the living trypanosomes.

W. Y.

Aoki (K.) & Kodama (H.). **Beitrag zur Frage der Immunisierung mit abgetöteten Trypanosomen.** [On the Question of Immunisation with Dead Trypanosomes.]—*Zeitschr. f. Immunitätsforsch. u. experim. Therapie.* 1913. July 26. Vol. 18. No. 6. pp. 693-700.

The question as to whether experimental animals can be immunised against trypanosome infections by dead trypanosomes is still undecided. A summary of the work which has been done along these lines is given. In their first series of experiments the authors attempted to immunise animals by means of a suspension of trypanosomes (*T. equiperdum*) which had been killed by formalin. Twelve rabbits were injected as follows:—Two animals 6 times at 6-12 day intervals with 1-2 cc. of the suspension and the other ten 3 times at 6-7 day intervals with 3 cc. Three of the animals died during the process. A week after the last vaccination all the remaining animals were inoculated with 1 cc. of virulent dourine blood; they all became

infected in a manner exactly similar to the controls. Eight rats and 17 mice were treated in a similar way with equally negative results. These experiments show that it is impossible to immunise small experimental animals by means of dead trypanosomes. As it was possible that the formalin material might not be satisfactory a further series of experiments were undertaken with dried trypanosomes. The trypanosomes were obtained from heavily infected rats by centrifugation of the citrated blood and after being once washed in normal salt solution were dried in an incubator at 37° C. for 20 hours; the mass was subsequently pulverised. Five rabbits, 10 rats and 10 mice were treated in a manner similar to that described above with the dried trypanosomes, but on subsequent inoculation with virulent blood they became infected in the ordinary way.

W. Y.

Oehler (R.). **Zur Gewinnung reiner Trypanosomenstämme.** [The Production of Pure Trypanosome Strains.]—*Centralbl. f. Bakt.* 1. Abt., Orig. 1913. July 29. Vol. 70. Nos. 1/2. pp. 110-111.

In a previous paper (see this *Bulletin*, Vol. 1, p. 525) the author showed that single trypanosomes could be separated in glass tubes and that experimental animals could be infected with them. He has carried out further experiments along these lines. A strain was carried on to the fourth passage by single trypanosome inoculation. The incubation and course of the disease remained the same. White mice injected with such a strain of *T. brucei* were treated with salvarsan and the salvarsan resistance of the strain was raised from ·4 mgm. to 5 mgm. The descendents of a chosen single trypanosome exhibited salvarsan resistance to just as great an extent as the strain carried on in the ordinary way. The capacity of resistance is, therefore, a general property of all individuals of the strain. Furthermore the salvarsan-fast strain was carried on by isolation and inoculation of a single trypanosome, and the resulting infection proved just as arsenic-fast as the previous strain.

An animal was infected with an arsenic-fast and a normal strain and the author succeeded by means of inoculating single trypanosomes in isolating both components.*

W. Y.

Schern (Kurt) & Citron (Heinrich). **Ueber Lävulosurie, sowie neuartige Serum- und Leberstoffe bei Trypanosomiasis.** [On Laevulosuria as well as new Serum and Liver Substances in Trypanosomiasis.]—*Deut. Med. Wochenschr.* 1913. July 10. Vol. 39. No. 28. pp. 1356-1357.

Reference is made to the previous work of Schern (*Sleeping Sickness Bulletin*, Vol. 4, p. 63) wherein it was shown that Dourine trypanosomes which had become immoble on mixing

* It has been suggested that the formation of fast strains is due to a process of selection, some individuals of the strain having been resistant from the first (Cockerell; Levaditi and Twort). Oehler's results show that this explanation will not hold, at any rate, for drug-fast strains.—A. G. B.

infected rat's blood *in vivo* with sodium citrate or normal saline solution regained their activity when fresh serum from a normal rat or horse was added. The observations recorded in the previous paper are confirmed; they were as follows:—

The length of time the trypanosomes remain motile outside the animal body depends on various factors, especially on the stage of the infection. Trypanosomes taken from an animal at the beginning of the infection may retain their motility for several hours at room temperature, whereas those obtained from an animal in the later stage of the disease, shortly before death, are much more labile and have as a rule lost their motility in 10-15 minutes. The length of time the parasites live *in vivo* is some criterion as to the probable duration of the animal's life: if the trypanosomes quickly lose their motility then it is to be expected that the death of the animal is imminent. The question arose as to whether only the serum possessed this life-prolonging property. Emulsions of liver were found to act similarly. Further experiments concerning the nature of the life-prolonging substances showed (1) that they are thermostabile, (2) that they withstand drying, (3) that they persist for a long time at 0° C. and at 37° C., and (4) that they are destroyed by putrefaction. The authors succeeded in obtaining extracts of liver and serum which contained the substance in question in concentrated form and which had been kept for four years at room temperature without losing its properties. The life-prolonging substance is not demonstrable in the serum of rats in a late stage of dourine infection, nor is it found in the fresh liver of rats which have succumbed from trypanosomiasis in the same amount as in the liver of normal animals. It was found that after treatment with atoxyl the substance—even if it had completely disappeared from the serum—gradually returned as the trypanosomes disappeared from the blood. If the animal remained cured the serum continued to be active, but if a relapse occurred the life-prolonging substance disappeared once more. It is suggested that by aid of this reaction the action of the remedy can be controlled.

Possibly these facts could be explained by a functional disturbance of the liver during trypanosome infection. Experiments were undertaken to decide the point. If animals with disease of the liver are fed with large amounts of laevulose this passes into the urine (alimentary laevulosuria); in normal animals this does not occur. As it is difficult to feed rats with a definite quantity of laevulose the sugar was administered intraperitoneally in physiological salt solution. Before proceeding with the experiments the largest amount of laevulose which could be administered to a healthy rat without the sugar appearing in the urine was determined. It was found that ·3 gm. of the sugar was always completely used up in the body of large rats. This amount was then given to a large number of infected animals. The urine of these rats in the earlier and middle stages of the disease was always free from sugar. On the other hand the urine of those animals in which the typanosomes remained motile only a short time in microscopic preparations and which were thus in the final stage of the disease, fermented on the addition of yeast. So soon as a definite reduction of the length of life of the trypanosomes of an infected rat occurs laevulose is passed in the urine after intraperitoneal injections of the sugar.

The authors write that through these experiments a new insight into the pathology of trypanosomiasis in rats is obtained. They are at present unable to state whether their experiments possess any significance for trypanosomiasis and spirillosis of

man and other animals than rats. It is also still to be demonstrated whether the diminution of the substance in question and the laevulosuria is specific for trypanosomiasis.

The conclusion is:—In rats suffering from trypanosomiasis (dourine, nagana or sleeping sickness) a functional disturbance of the liver can be demonstrated in the last stages of the infection.

W. Y.

Fry (W. B.) & Ranken (H. S.). **Further Researches on the Extrusion of Granules by Trypanosomes and on their Further Development. (With a Note on Methods by H. G. Plimmer).**—*Proc. Roy. Soc.* 1913. June 12. Vol. B. 86. No. B. 589. pp. 377-393. With 3 plates.

The methods used by the authors were (1) dark ground illumination and (2) "vital staining" with ·75 per cent. toluidine blue in physiological salt solution. Methods of fixation devised by Plimmer were followed. The trypanosomes used were *T. gambiense* (Sudan), *T. rhodesiense*, *T. brucei*, *T. evansi* (Sudan), *T. nanum* (Sudan), *T. pecaudi* (Sudan), *T. lewisi*. Two classes of granules were distinguished:—(1) Infective vital granules, probably of nuclear origin; (2) others, non-infective and probably nutritive. Infective granules only were considered.

In all cases the granule, as seen by dark ground illumination, is small, sharply defined, highly refractile. With toluidine blue it stains deeper than the rest of the trypanosome body. The "sequence of events during an exacerbation" of trypanosomiasis is:—"(1) Trypanosomes without granules. (2) Trypanosomes showing granules which gradually become larger and very evident. (3) Many free granules. (4) Many trypanosomes but no contained granules. (5) Trypanolytic crisis or death of the animal." The mechanism of extrusion of granules was studied in *T. nanum* and *T. gambiense*. In the latter, the granules are multiple, move backwards and forwards in the long axis of the organism and are usually extruded from some point near the middle of the body. Extrusion of granules can be stimulated by drugs or mechanical effects, e.g. variations in osmotic conditions. Usually extrusion of granules does not seem to have a prejudicial effect on the trypanosome as seen in warm, wet preparations. "Extrusion of granules, if occurring generally, apparently heralds the disappearance of trypanosomes from the blood." Three methods by which granules may be liberated are described.

In animal infections and in human cases of sleeping sickness granules are found in the blood, glands and internal organs. Regarding further development of the granules, the authors state that "further stages are more difficult to follow, as all stages cannot be seen in any individual preparation." Elongation occurs, a Leishmania-like form being produced. "Death in acute trypanosomiasis is caused by plugging of the cerebral capillaries with these forms." Each Leishmania-like body may then elongate direct, or schizogony may occur prior to the assumption of the flagellate form. Enormous numbers of these small bodies occur in the internal organs, especially in the lungs.

Granules free from trypanosomes were obtained by mixing infected blood with hypertonic salt solution up to 2 per cent., one volume of blood with 2 or 3 of salt being used, and maintained at 34° C. to 38° C. Gerbils inoculated with such granules of *T. nanum* became infected.

Plimmer's fixation, involving the use of iodine as a vapour or in solution, is necessary for demonstrating these granules to advantage.

[Regarding these interesting observations, a short comment may be added on the rounded forms of trypanosomes. Such were described by Moore and Breinl (1907), and by Fantham (1911), the latter worker definitely comparing the rounded forms with *Leishmania.* They were considered as part of the trypanosome cycle in the vertebrate host. These views have been criticised in a somewhat unduly severe manner, apparently because Laveran and Mesnil in 1903 considered some rounded bodies to be "involution" forms. But Fantham showed that Leishmania-like forms of *T. gambiense* and *T. rhodesiense* were infective to experimental animals, and Laveran confirmed this, though still interpreting the rounded bodies as involution forms. Some trypanosomes, when degenerating, become rounded, but their nuclei show some degeneration phenomena. The mistake has been made by some of generalising that all rounded forms are the same and all are degenerate. Rounded Leishmania-like forms are known to be definite cyclical stages in a number of nearly allied genera of flagellates, and it now remains not only to confirm the interesting results of Fry and Ranken, but also to test their applicability to other organisms].

A. Porter.

Bonger (C.). **Über die Morphologie und das Verhalten der von P. Behn in deutschen Rindern nachgewiesenen Trypanosomen bei künstlicher Infektion.** [On the Morphology and the Behaviour of the Trypanosome described by P. Behn in German Cattle on Artificial Infection.]—*Zeitschr. f. Hygiene u. Infektionskr.* 1913. July 17. Vol. 75. No. 1. pp. 101-117. With 1 plate.

The paper commences with an account of the previous work on *T. theileri* and allied trypanosomes. Reference is made to the work of Behn (*Sleeping Sickness Bulletin* Vol. 4, p. 111.).

The parasite found by Behn in German cattle and maintained by the author by passage through calves exhibits three chief forms —long slender varieties, large broad varieties and short slender varieties. Its length is 20-70 microns and its breadth 2-6 microns. Only cattle were successfully inoculated with the parasite; sheep, goats, rabbits, guinea-pigs and mice were refractory, and as Behn has shown not all cattle are susceptible. The average incubation period was 7 days. A febrile reaction was observed before trypanosomes appeared in the peripheral blood. The average maximum temperature of all experimental animals was 40·3° C. Beyond the temperature no symptoms were observed.

The author compares his experimental results with those of Theiler and comes to the conclusion that *T. theileri* (Bruce and Laveran) and that discovered by Behn in German cattle must, if they are not identical, be very closely related.

W. Y.

Carpano (M.). **Trypanosomen vom Typus des *Tr. Theileri* in den Rindern der Kolonie Erythräa.** [Trypanosomes of the *T. theileri* Type in Cattle in Erythrea].—*Centralbl. f. Bakt.* 1. Abt. Orig. 1913. Aug. 23. Vol. 70. No. 5-6. pp. 209-217. With 1 plate.

Systematic examination of the blood of sick cattle in Erythrea revealed not uncommonly the presence of a trypanosome of the *Theileri* type. The following are the conclusions:—

In cattle of Erythrea a large trypanosome is found belonging to the *Theileri* type.

It is not found alone, but is generally associated with *Pir. bigeminum, Pir. mutans, Anaplasma marginale, T. abyssinicum, Sp. bovis* and is most frequently found in cattle sick of rinderpest.

The clinical picture varies and is dependent on the accompanying disease; not uncommonly it presents the features of Galziekte or gall fever.

The parasite can be cultivated in the Novy-McNeal medium (a mixture of agar with the defibrinated blood of an infected ox). In cultures the parasites acquire a peculiar morphology approximating to *Herpetomonas* and *Crithidia.*

The cultures die out after about 20 days, owing to degeneration of the parasites.

Transmission through inoculation of infected blood does not always succeed in the cattle of Erythrea. The inoculated cattle must be susceptible for the parasites which in general accompany this trypanosome, especially *Piroplasma bigeminum.*

W. Y.

Rondoni (P.) & Goretti (G.). **Ricerche Sperimentali sul Nagana. i. Communicazione. Su alcune Proprietà Biologiche della Milza nella Infezione Sperimentale da *Trypanosoma brucei*.** [Experimental Researches on Nagana.]—*Lo Sperimentale.* 1913. April 7. Vol. 67. No. 1. pp. 1-24.

The authors of this paper give an account of experiments which they undertook in order to study certain properties of the spleen of guinea-pigs, rats and mice during the course of an infection with *Trypanosoma brucei.* They endeavoured to demonstrate the presence of trypanocidal substances and specific antigens in the spleen, and also studied its haemolytic powers.

A description of the technique adopted for each portion of their experiments is given in detail.

In the spleen there is sometimes a certain degree of special trypanolytic power; the spleen must have a certain importance in the defence of the organism, it is something more than a simple filter in which accumulate fragments of trypanosomes already dead. However, it appears not to have in it a marked accumulation of trypanosomal antigens such as one might use, for example, for experiments and attempts at immunisation.

Aqueous extracts of the spleen of infected animals possess a definite haemolytic power on erythrocytes of whatever origin

(even from the same individual); two active substances can be extracted by alcohol; they behave irregularly as regards heat; they are capable of being inhibited, in part at least, by normal serum; they are probably of lipoid nature and have but slight importance during life.

W. Y.

Aragao (Henrique de Beaurepaire). **Nota sobre as Schizogonias e Gametogonias dos Trypanosomos.**—*Brazil Medico.* 1913. July 15. Vol. 27. No. 27. pp. 271-272.

The paper consists of a review of the results obtained by various workers on the schizogony of different trypanosomes, following the discovery of that process in *Trypanosoma cruzi* by Chagas, together with criticisms of the same.

Aragao professes a certain amount of scepticism with regard to the connection of the pulmonary cysts, usually considered as multiplicative stages of *T. cruzi*, and the flagellate of Brasilian trypanosomiasis. In his experiments, schizogonic cysts occurred in normal animals; 8 out of 31 dogs, 11 out of 46 guinea-pigs and 2 out of 7 rats containing them. This was confirmed by Delanoë who also found them in other animals in which no trypanosomes, as such, were present. Delanoë thinks that the pneumocysts may belong to the Coccidia, while Tizzer thinks they are Cryptosporidia. In some animals, pneumocysts appear to produce no pathological alterations and seem to be inoffensive to the host.

A. P.

Strachan (Henry). **West African Notes. (1) Note on a Portable Insect-proof Room. (2) Notes on the Bites of the Tsetse-Fly (*Glossina palpalis*).**—*Jl. Trop. Med. & Hyg.* 1913. July 15. Vol. 16. No. 14. p. 214.

1. Note on a portable insect-proof room, constructed by Messrs. Conner and Sons, 263, Lewisham High Road, S.E.

2. Notes on the bites of *Glossina palpalis*. The attack of the fly varied strangely. It was sometimes accompanied by a loud buzz and violent impact, with a sharp and painful stab. At others it was silent and painless, and it not unfrequently happened that only the discovery that blood was staining the site of the puncture revealed the fact that one had been bitten. The author is of opinion that there is grave danger of sleeping sickness spreading southward along the river valley into the western province of Southern Nigeria.

W. Y.

RELAPSING FEVER.

Marchoux (E.) & Couvy (L.). **Argas et Spirochètes. (Premier Mémoire.)**—*Ann. Inst. Pasteur.* 1913. June. Vol. 27. No. 6. pp. 450-480. With 15 text-figs.

This first part of this interesting memoir is devoted to a historical account of Leishman's granules, first observed by Dutton and Todd in the Malphigian tubules of *O. moubata* infected with *S. duttoni*, and subsequently by Leishman, Balfour, Hindle, and Fantham. The authors then proceed to discuss the origin of the granules, which are stated to be derived from the breaking up of little masses of protoplasm occurring in the cells of the Malphigian tubules, ovules, and the genital canals of the male and female.

When fully formed, the granules are ovoid bodies about 0·5 × 1μ and are agglomerated into large masses simulating schizogony. In the Malphigian tubules they may become so numerous as to completely fill the cytoplasm of the cells, but in the ovules and cells of the genital ducts the granules are less numerous, occurring in little groups, or sometimes singly. The shape of the granules is not constant, for, especially in the genital ducts, they are sometimes bacilliform.

The authors then consider the question of the relation of the granules to the spirochaetes. In the first place the disappearance of spirochaetes from the tick is more apparent than real. (See this *Bulletin*, Vol. 1, p. 395.) By staining with gentian violet it is possible to detect spirochaetes in the coelomic fluid of ticks submitted to the following processes:—(1) Starvation for forty-five days at 28° C., and (2) for eleven months at 15° C. In the latter case attenuated spirochaetes could still be found in small numbers in the coelomic fluid, and more or less normal spirochaetes in the salivary ducts and the interior of the palps. (3) Five months starvation, the ticks being kept alternately in the ice-chest and the laboratory.

In addition, attempts were made to cause the disappearance of spirochaetes from the body of the tick, by feeding it on a fowl hyperimmunised against *S. gallinarum*, but this procedure was without effect. The direct inoculation of hyperimmune serum into the body cavity of Argas caused the spirochaetes to disappear for the moment, but in three-fifths of the cases the parasites reappeared after a few days.

The thickness of the spirochaetes diminishes when the ticks are starved, but the normal dimensions are recovered after the tick has ingested blood. Employing *Hindle's method certain Argas were fed on normal saline, after which it was found that the attenuated spirochaetes were quite unaffected in thickness. Moreover, some ticks were fed on blood and others, of the same lot, on normal saline. Spirochaetes were excessively rare and

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* Hindle & Merriman. The Sensory Perceptions of *Argas persicus* (Oken). —*Parasitology.* 1912. Vol. 5. pp. 203-216.

were extremely slender in the coelomic fluid of the latter, whilst as many as ten normal spirochaetes could be found in a drop of coelomic fluid from those ticks that fed on blood. These attenuated spirochaetes are said to be virulent, for when injected into fowls they produced infection.

The authors were able to observe the rapid passage of the spirochaetes from the gut through the gut wall into the coelomic fluid, thus confirming HINDLE's observations. Certain of the spirochaetes, however, remain in the lumen of the gut, disappearing eight to twelve days later. During this period the spirochaetes break up into granules, and also short spirilla may be found, but these are to be regarded as merely degeneration forms.

With regard to the nature of LEISHMAN's granules the authors are unable to give a definite opinion but bring forward evidence to show that they are not a stage in the development of the spirochaete. When the bodies are maintained at a temperature of about 37° C., they were observed to elongate and assume bacilloid and spirilloid forms, but without ever becoming transformed into normal spirochaetes. Moreover the granules may be found in the Malphigian tubules of *Argas vespertilionis, Rhipicephalus sanguineus, Haemaphysalis concinna, Amblyomma variegatum, Dermacentor reticulatus, Ixodes ricinus*, and *Lelaps echidninus*.

The authors' conclusions are as follows:—

(1) In *Argas persicus* granules are present similar to those described for the first time by LEISHMAN in *O. moubata*.

(2) These granules have no relation to the spirochaetes.

(3) It is impossible to inoculate them into an animal without at the same time inoculating spirochaetes.

(4) We have found spirochaetes in the coelom of all the *A. persicus* that we have examined.

(5) These spirochaetes are often so fine that they are not colourable by Giemsa, but may be put in evidence by staining with gentian violet.

(6) There are other spirochaetes so fine that they remain invisible whatever the staining method employed.

(7) We have not succeeded in obtaining Argas free from spirochaetes.

(8) A large number of the spirochaetes ingested by the Argas almost immediately pass through the wall of the alimentary canal and appear in the coelomic fluid.

(9) Those which remain in the gut degenerate in eight to twelve days.

(10) The fragmentation of the chromatin in the spirochaetes must not be considered as a transformation of these organisms into granules, but as a process of degeneration.

(11) Leishman's granules differ from spirochaetes in a large number of characters and reactions.

(12) They exist normally in numerous acariens.

(13) We have not observed any changes in the spirochaetes whilst in the invertebrate host, permitting one to cease from regarding these parasites as bacteria.

[This important memoir should be read in its entirety by those interested in the nature of spirochaetes and their life-cycle within their respective hosts. The evidence brought forward by the authors seems to suggest that the granules have no relation to spirochaetes.]

E. Hindle.

Mackie (F. P.). **The Body-louse (*Pediculus vestimenti*) as a Disease Carrier. The Body-louse as a Carrier of Relapsing Fever.**—*Proceedings of the Third Meeting of the General Malaria Committee held at Madras,* Nov. 18, 19, 20, 1912. pp. 281-289. (1913. Simla: Govt. Central Branch Press.)

The present article is an interesting summary of our knowledge of the body-louse as a disease carrier and is divided into three parts, the first of which is concerned with the body-louse as a carrier of relapsing fever, the second with the body-louse as a carrier of typhus fever, and a third part with the bionomics of the body-louse. In the first part the author recalls his observations made during the Nasik epidemic of Indian relapsing fever (*S. carteri*) in August, 1907.* It may be noted that this outbreak occurred in a mission settlement amongst a juvenile population. It broke out in the boys' ward and in about one month 137 out of 145 boys were struck down. Later it spread to the girls' ward but there it only progressed very slowly and ultimately only 35 out of 115 girls became infected. The boys were swarming with body-lice whilst these parasites were much less common on the girls; on the other hand, bugs were very abundant in the girls' ward but were absent from the boys' quarters. On dissecting the lice obtained in the wards during the height of the epidemic, out of 112 from the boys' ward, 24·1 per cent. were infected with spirilla whilst out of 29 obtained from the girls' ward only one was infected.

The chief seat of the multiplication of the spirochaetes appears to be the alimentary canal, and Mackie thinks it possible that the infection travels forward to the pharynx and mouth-parts of the louse. About 100 eggs were examined but no spirilla found.

The remainder of this section and the next, dealing with the body-louse and typhus fever, consist of a summary of the more important literature on the subject.

In the section dealing with the bionomics of the body-louse the author gives short notes on the anatomy and breeding habits of these insects. In India both eggs and adults do best in a cool incubator. The length of life of the adults was found to be only about 7-10 days, but the insects were only fed once a day and Warburton† states that it is necessary to feed them twice a day in order to keep them in good health.

Over 100 head-lice from infected boys and girls were examined at Nasik, but no blood was ever found in the insects, their only food seeming to be a greasy sebaceous material. It is noted, however, that Patton found blood in head lice.

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* Mackie: The Part played by *Pediculus corporis* in the Transmission of Relapsing Fever.—*Brit. Med. Jl.* 1907. Dec. 14. pp. 1706–1709.

† Warburton: A Preliminary Investigation on Flock as a possible Distributor of Vermin, and on the Life History of the Body-louse (*Pediculus vestimenti*).—*Repts. to the Local Govt. Board on Public Health & Medical Subjects.* 1909. New Series No. 2. p. 3; also 1910. New Series No. 27. p. 25.

The author recalls that he first observed the flagellate occurring in the body-louse and subsequently described by FANTHAM as *Herpetomonas vestimenti*. The presence of this flagellate must be remembered by those investigating the disease carrying power of the louse, especially in kala azar. In Madras last May the author fed 279 body-lice on patients suffering from this disease who had *Leishmania donovani* in their peripheral blood. On subsequently dissecting the lice at different intervals no flagellates of any sort could be found.

Finally it is pointed out that the body-louse is one of the easiest of all blood-sucking parasites to eradicate, for personal cleanliness and the disinfection or even plain washing of clothes is sufficient to kill the lice, especially if the garments are afterwards exposed to the sun to dry. It is probable that the isolation of patients together with the disinfection of clothes and bedding, and the avoidance of actual contact, will suffice to cut short epidemics of relapsing fever and typhus.

[Without wishing in any way to detract from the credit due to Captain Mackie for his important observations, his opening statement that "the first record of the louse being suspected as a carrier of a specific disease dates from the publication of the observations made at Nasik in August 1907 on an epidemic of Relapsing Fever," is not strictly accurate. As far back as 1891 FLÜGGE* suggested that lice were responsible for the transmission of European Relapsing Fever. Moreover, with regard to other infections DEWÈVRE (1892)† performed experiments proving that impetigo was carried by lice, whilst AUBERT (1879)‡ considered that these parasites caused impetigo, prurigo, pityriasis, etc., and especially favus.]

E. H.

TODD (John L.). **A Note on the Transmission of Spirochaetes.**—*Proc. Soc. for Experim. Biology & Med.* 1913. April. Vol. 10. No. 4. pp. 134-135. [87 (783).]

On several occasions the author has examined the coxal and anal fluids excreted by infected *Ornithodorus moubata* coming from Uganda and British Central Africa. In every instance the fluid was taken while the ticks fed upon an uninfected animal. The fluid collected was free from blood and in two instances coxal fluid was obtained free from anal secretion. On six occasions, after the fluid had been centrifuged, spirochaetes morphologically identical with *S. duttoni* were found in it. In addition spirochaetes were found in the fluid that apparently contained no anal secretion.

[Dr. Todd's observation is the first record of spirochaetes, as such, being found in the coxal fluid and anal secretions and is

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* FLÜGGE C. (1891) Grundriss der Hygiene. pp. 473 and 532.

† DEWÈVRE (1892) Note sur le Rôle des Pediculi dans la Propagation de l'Impétigo.—*Compt. Rend. Soc. Biol.* Paris. 1892. No. 11. pp. 232–234.

‡ AUBERT (1879) Les Poux et les Écoles. Un Point d'Hygiène Scolaire. Lyon, 1879. Reviewed in *Ann. de Dermatologie et de Syphiligraphie*, 1880. 2 ser. vol. 1. p. 292.

of considerable interest in view of Leishman's suggestion that, when a tick feeds, the infection is produced by the entrance of these fluids into the open wound caused by the tick's bite.]

E. H.

Jukes (A. M.). **Spirillar Fever in the Darjeeling District, 1912.**—*Indian Med. Gaz.* 1913. June. Vol. 48. No. 6. pp. 222-225.

The present article contains a more detailed account of a spirillar fever occurring in the Darjeeling District, which was previously described by the author (see this *Bulletin*, Vol. 1, pp. 387-388). In every case the illness is severe. The temperature is irregular and shows no resemblance to that of relapsing fever, and no relapses have been observed in the case of those that recovered. The author is inclined to regard the fever as hitherto undescribed, and adds some notes by Capt. Mackie on the morphology of the spirochaete causing the disease. The parasites tend to group themselves into two ranges, the shorter from 9-11μ, and the larger from 15-18μ in length, and this is what often happens in the Bombay form. On the whole, however, they appear to be somewhat shorter than the type specimens of *S. carteri*, but this is not a very reliable guide. Lice and bugs from infected houses were dissected, but in no cases were spirochaetes found in any of these insects.

The author adds some further observations by Sub-Assistant Surgeon Swole who at Kurseong in June saw five cases of similar fever with two deaths in people who had recently come from Tibet. Spirochaetes were found in the blood of one of them, so it seems probable that this fever also occurs in Tibet. In addition the coolies of the Takvar Estate stated that the fever is well-known in Nepaul and that it is very fatal, but if a patient lives till the eighth day he generally recovers. The author heard on reliable information that in another epidemic on a tea-garden, twenty out of twenty-one persons died. The disease was still continuing in December. In the appendix detailed symptoms of three cases are given.

E. H.

Rizzuti (G.). **Osservazioni sul Tifo Ricorrente a Tripoli.** [Observations on Relapsing Fever in Tripoli.]—*Malaria e Malat. d. Paesi Caldi.* 1913. April-May. Vol. 4. No. 3. pp. 153-172.

During the first period of the Italian military occupation of Libya, from December 1911 to March 1912, the author observed 25 cases of relapsing fever among the soldiers. In all cases the clinical symptoms resembled those described for the relapsing fevers of other parts of North Africa, but were rather mild, for none of the patients succumbed to the disease, though no medicaments were employed.

Detailed descriptions are given of the clinical symptoms of the disease in sixteen of the patients, but none of them call for any special notice. Icterus was noticed in ten per cent., vomiting in 50 per cent., epistaxis in 25 per cent., haematuria in three per cent., splenomegaly in 80 per cent., and enlarged liver in 15 per cent. of the cases. During the fever there was a decrease in the percentage of haemaglobin, and the number of "Rossi's corpuscles," accompanied by a well marked increase in the number of leucocytes. The spirochaetes were never very numerous in the blood, not more than 1-2 per microscopic field, and agglutinated masses of the parasites were never observed. In defibrinated blood at ordinary temperature the spirochaetes remained motile for seven days; and in hanging drop preparations for three to four days. Mice were infected by the subcutaneous injection of 1 cc. of the blood from an infected patient, but the results of the experimental work with animals are reserved for a future communication.

The author adds that all the cases of relapsing fever, as well as those of typhus (some of which also occurred amongst the troops), agree with the view that lice are responsible for the transmission of the infections.

E. H.

Kusunoki (F.). **Experimentelle Untersuchungen über Heredo-Immunität bei afrikanischer Recurrens und über den etwaigen Einfluss von Immunitätsvorgängen auf die Wirksamkeit eines chemotherapeutischen Mittels.** [An Experimental Investigation of the Inheritance of Immunity in African Relapsing Fever and the Possible Influence of Immunity on the Action of Chemotherapeutic Substances.]—*Zeitschr. f. Chemotherapie.* 1. Abt., Orig. 1913. Vol. 2. No. 1. pp. 11-22.

Working with a very virulent strain of *S. duttoni*, the author found that rats and mice that had recovered from an infection could not be reinfected after an interval of two months. Young rats born whilst the mother was infected or after she had recovered from an infection were found to be quite susceptible when inoculated subcutaneously with the same virus. It seems, therefore, that in the case of infections of *S. duttoni* no immunity is transmitted to the offspring.

In order to test the possible influence of immune substances on the action of salvarsan the author inoculated fifteen mice with *S. duttoni*. Five of these were used as controls and all died; six were injected on the second day with 1 cc. of a 1/900 solution of salvarsan per 20 mgm. body weight, whilst of the remaining four mice, two were injected with the same dose on the fourth day of the infection and two on the sixth day. Three of those treated on the second day of infection recovered, whilst all the others succumbed, so that the presence of immune substances does not seem to influence the action of the drug. It should be noted that, according to Hata, the smallest curative dose for

S. duttoni in mice is 1 cc. of a 1/700 to 1/800 solution of salvarsan per 20 gm. body weight and the author purposely used a smaller dose in order to detect whether the presence of immune substances had any effect. The results of this and also two other experiments, in which the salvarsan was administered prior to the infection, show that in the case of infections of *S. duttoni* the action of this compound is not in any way affected by development of any natural immunity in the host.

E. H.

Chambers (Helen). **A New Spirochaeta found in Human Blood. Preliminary Communication.**—*Lancet.* 1913. June 21. pp. 1728-1729. With 5 text-figs.

The author claims to have found spirochaetes in the blood of a number of persons both healthy and unhealthy. A total of 47 cases was examined and the organism detected in all except three.

The blood was collected in small Wright's tubes and allowed to clot at 37° C. for twenty minutes. The serum was then pipetted off and the remainder of the clot returned to the incubator; after 1½ hours the serum which separated, owing to further shrinkage, was examined by dark-ground illumination. The organisms are said to escape into the serum chiefly during the last stage of contraction of the clot.

The organism is said to be variable both in length and thickness, to multiply by longitudinal division and to frequently show round spore-like bodies attached to the ends or laterally. With Giemsa and Leishman's stain small red chromatic granules are often found at the end and sometimes along the length of the body; the rest of the spirochaete stains faintly blue.

Various attempts to cultivate the organism are also described, but although it multiplies in the blood itself or in the first cultures, no subcultures could be obtained. "A broth tube containing these organisms was heated to 50° C. for an hour. They were still actively motile." (!)

[The appearances figured by Dr. Chambers have merely a very superficial resemblance to spirochaetes and from the description there can hardly be any doubt that the author has been misled by the very extraordinary appearances assumed by degenerating and coagulated blood.]

E. H.

Sangiorgi (Guiseppe). **Spirochetosi della Cavia.** [Spirochaetosis of the Guinea-pig.]—*Pathologica.* 1913. July 15. Vol. 5. No. 113. pp. 428-430. With 3 text-figs.

Whilst performing the autopsies of numerous guinea-pigs that had been infected with "Guinea-pig plague," the author on one occasion discovered a spirochaete which is apparently pathogenic. The parasite was found inhabiting the cavities of various lesions

of the liver and seemed to be mainly responsible for certain inflammatory and degenerative changes that had taken place. The spirochaetes belonged to two types, the first of which measured 3·2μ to 4·8μ in length by 0·3μ to 0·4μ in breadth, whilst the larger forms were 9·6μ to 11·2μ in length and about the same breadth as in the other type. The relations between these two types could not be decided, and also the author did not observe any traces of division. Attempts at subinoculations failed, since the guinea-pig infected with spirochaetosis had died as a result of the Guinea-pig plague, and therefore all animals inoculated from it died as a result of the latter disease before any spirochaetes could be detected.

This spirochaete, for which the name *Spiroschaudinnia caviae* is proposed, seems to be identical with that also observed in the guinea-pig by De Gasperi. [See this *Bulletin*, Vol. 1, p. 396.]

E. H.

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(Telephone :—Kensington, 5188.)

Books Received.

von Hoffmann (Géza). Die Rassenhygiene in den Vereinigten Staaten von Nordamerika. [Race Hygiene in the United States of America.]—xii + 237 pp. With 1 text-fig. 1913. München: J. F. Lehmanns Verlag. [Paper cover 4 Mk.; bound 5 Mk.]

[The contents of this book are indicated by the headings of the chapters: The ground laws of race hygiene; The spread of ideas of race hygiene in the United States; The regulation of marriage in the race hygiene sense; The sterilisation of degenerates; The selection of immigrants. The second half of the work is occupied by extracts from the laws of the several States which bear on these topics and a classified list of 700 publications, most of which are in the English language.]

Luys (Georges). A Text-Book on Gonorrhea and its Complications. Translated and edited by Arthur Foerster. — xx + 384 pp. Roy. 8vo. With 3 coloured plates and 200 text illustrations. 1913. London: Baillière, Tindall & Cox. [15*s.* net.]

[A well-illustrated and clearly printed work giving a complete account of the common disease of which it treats. The translation is from the second French edition, the first having been published in 1912.]

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